GHENT UNIVERSITY

FACULTY OF MEDICINE AND HEALTH SCIENCES

Care for potential donors after brain death in Belgium: the present and recommendations for the future

Pieter Hoste

2019

Promotors

Prof. dr. Koenraad Vandewoude

Prof. dr. Kris Vanhaecht

Thesis submitted to fulfill the requirements for the degree of Doctor in Health Sciences

Care for potential donors after brain death in Belgium: the present and recommendations for the future.

Pieter Hoste

Doctoral thesis. Ghent University, Ghent, Belgium

ISBN: 9789463882118

Printed by University Press

This project was supported by a grant offered by the Belgian Federal Public Service Health, Food Chain Safety and Environment, Victor Hortaplein, 40 bus 10, 1000 Brussels.

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Promotor

Prof. Dr. Koenraad Vandewoude

Department of Internal Medicine and Pediatrics, Ghent University, Belgium

Co-promotor

Prof. Dr. Kris Vanhaecht

Leuven Institute for Healthcare Policy, Department of Public Health and Primary Care, KU Leuven - University of Leuven, Belgium

Members of the doctoral advisory committee

Prof. Dr. Xavier Rogiers

Department of Human Structure and Repair, Ghent University, Belgium

Prof. Dr. Kristof Eeckloo

Department of Public Health and Primary Care, Ghent University, Belgium

Members of the examination committee

Prof. Dr. Johan Van de Voorde, Chair of the Examination Board

Department of Basic and Applied Medical Sciences, Ghent University, Belgium

Prof. Dr. Rik Verhaeghe

Department of Public Health and Primary Care, Ghent University, Belgium

Prof. Dr. Ann Van Hecke

Department of Public Health and Primary Care, Ghent University, Belgium

Prof. Dr. Kirsten Colpaert

Department of Internal Medicine and Pediatrics, Ghent University, Belgium

Prof. Dr. Walter Sermeus

Leuven Institute for Healthcare Policy, Department of Public Health and Primary Care, KU Leuven - University of Leuven, Belgium

Prof. Dr. Peter Van Bogaert

Department of Nursing and Midwifery Sciences, University of Antwerp, Belgium

Prof. Dr. Philippe Jorens

Department of Critical Care Medicine, University of Antwerp, Belgium

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List of abbreviations

AAN	American Academy of Neurology
AGREE	Appraisal of Guidelines for Research & Evaluation
BTS	Belgian Transplantation Society
CPGs	Clinical Practice Guidelines
cRCT	Cluster Randomized Controlled Trials
DBD	Donor after Brain Death / Donation after Brain Death
DCD	Donor after Circulatory Death / Donation after Circulatory Death
EDHEP	European Donor Hospital Education Program
ETPOD	European Training Program on Organ Donation
EU	European Union
ICU	Intensive Care Unit
IPA	Importance-Performance Analysis
NICE	National Institute for Health and Clinical Excellence
IQR	Interquartile Range
KI	Key Intervention
MeSH	Medical Subject Headings
ODEQUS	Organ Donation European Quality System
OTPD	Organs Transplanted Per Donor
QAPs	Quality Assurance Programs
QI	Quality Indicator
RQ	Research Question
SD	Standard Deviation
UNOS	United Network for Organ Sharing

Chapter 1

Introduction

1. Introduction

Organ donation and transplantation in Belgium

The Belgian transplantation law

In Belgium, organ donation and transplantation is regulated by the law of 13 June 1986, which has been significantly modified since then. The explanatory memorandum accompanying this law explains its two important purposes: on the one hand to safeguard the respect for the body's personal rights by an explicit and precise legislation and on the other hand to develop efficiently a socially necessary part of the Belgian healthcare system [1]. For deceased donation, the Belgian legislator installed an opting-out system, meaning that each citizen is a potential organ donor. The opting-out system also provides on top of the basic universal consent to donation for all Belgian citizens the possibility to register actively either "for" or "against" organ donation. Active registration as a potential donor is encouraged, e.g. through city councils or even in the context of elections. This law does not explicitly define the criteria to be used for the determination of death of the donor but mentions that the criteria should be based on the latest medical knowledge concerning the subject. Therefore, in addition to donation after brain death, donation after circulatory death is legal in Belgium. Death of the donor must be certified by 3 physicians, excluding those who are treating the receptor or will perform the procurement or transplantation. The Belgian transplant law also guarantees anonymity and the absence of contacts between the donor and recipient families [1, 2]. Access to the Belgian transplant waiting lists is limited to candidates registered in the Belgian population register (or in the foreigner's register for at least six months), or to candidates not included in both registers who have been officially registered as residents in a Eurotransplant country for a period of more than 6 months. By renewed contracts, the Belgian authorities have delegated the organization of organ allocation and cross-border exchange of deceased donor organs to Eurotransplant, which covers, besides Belgium, also the Netherlands, Austria, Croatia, Germany, Hungary, Luxembourg

and Slovenia. Allocation rules are defined by Eurotransplant and regularly updated in accordance with the advice of the organ-specific committees and after final approval by the Belgian Federal Public Service Health, Food Chain Safety and Environment. The Belgian transplantation law also allows organ procurement, such as a kidney or portion of a liver, from informed living donors. Of note, the Belgian transplantation law forbids any financial remuneration for deceased or living organ donation [2].

Organization of organ donation, procurement and transplantation in Belgium

Each general hospital with a recognized intensive and emergency care unit in which organ retrieval from deceased donors takes places, has installed a local donor coordination function. This function includes the organization of those activities that facilitate the detection of potential donors and appropriate donor management, guaranteeing traceability of organs, and organizing local training courses on organ donation. This function should be performed by a multidisciplinary team consisting of at least one nurse and one specialist physician with a special professional title in intensive care. One physician and one nurse in this team are responsible for its coordination. These donor coordinators have clearly defined responsibilities in establishing, managing and reviewing the deceased donation processes in their hospital [3].

As soon as a donor is detected on an emergency ward or intensive care unit, this donor coordination function informs the transplant coordinator of the reference transplant center, with whom a cooperation agreement was concluded between institutions. These transplant coordinators ensure coordination during organ allocation and procurement. All seven university hospitals and one non-university hospital (OLV Hospital Aalst, only for heart transplants) have a transplant center and have been accredited to perform deceased and living transplantation in Belgium.

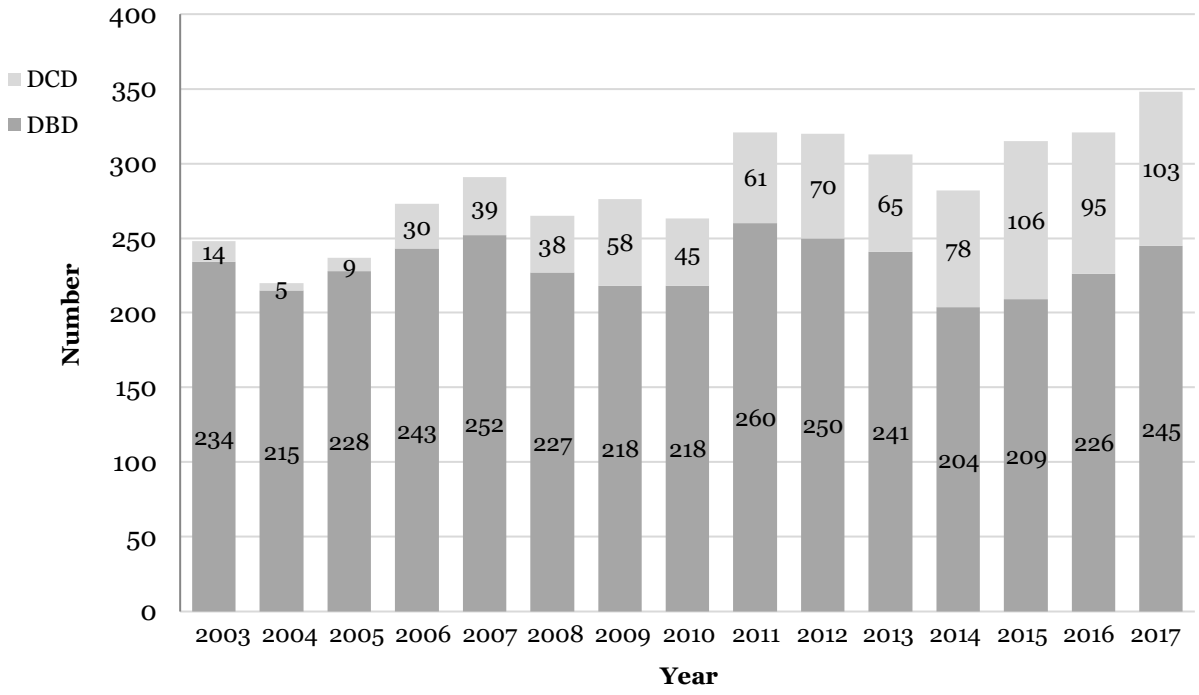
Donation and transplantation activity

The majority of solid organ transplantations performed in Belgium originate from deceased organ donors (Table 1). In part due to one of the world's highest deceased donation rates (between 24.3 and 30.6 deceased donors per million inhabitants from 2008 to 2017, 30.6 in 2017), living donation represents a limited share of the overall transplantation rates (11.5% for kidneys, 13.4% for livers in 2017) and partly serves for patients without possible access to the deceased donor waiting list [4].

Table 1: Transplantation activity in Belgium between 2008-2017 [4]

	2008	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**
Deceased donor										
Kidney	442	428	404	474	480	435	387	480	453	485
Heart	75	68	68	76	77	75	82	82	70	79
Lung	82	90	114	111	129	101	104	114	129	121
Liver	199	208	207	255	250	248	221	247	255	260
Split liver	18	12	3	7		2	10	4	1	9
Pancreas	19	13	22	18	13	8	11	9	11	14
Intestine	2	1	0	4	2	0	4	0	0	3
Pancreatic islets	12	12	7	15	19	9	7	11	12	8
Subtotal	849	832	825	960	970	878	826	947	931	979
Living donor										
Kidney	45	49	49	40	57	63	68	57	67	63
Domino Liver	0	2	0	2	2	0	2	1	3	3
Liver	13	23	33	35	30	42	38	32	43	33
Subtotal	58	74	82	77	89	105	107	90	113	99
Total	907	906	907	1037	1059	983	933	1037	1044	1078

The majority of deceased organ donors are donors after brain death (DBD). In 2017, out of 348 utilized deceased organ donors respectively 245 (70.4%) were DBD and 103 (29.6%) donors after circulatory death (DCD). Over the past 10 years, the percentage of controlled DCD (cat III, IV and V) to the pool of deceased donor organs has substantially increased to reach 29.6% in 2017. In contrast, uncontrolled DCD (cat I and II) is rarely performed in Belgium (Figure 1).



	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Total DBD	**234**	**215**	**228**	**243**	**252**	**227**	**218**	**218**	**260**	**250**	**241**	**204**	**209**	**226**	**245**
DCD Cat I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DCD Cat II	1	0	3	2	1	1	1	3	3	1	0	0	0	0	0
DCD Cat III	11	5	4	26	37	37	55	40	56	64	62	74	96	89	98
DCD Cat IV	2	0	1	1	0	0	0	1	1	2	0	0	2	1	0
DCD Cat V	0	0	1	1	1	0	2	1	1	3	3	4	8	5	5
Total DCD	**14**	**5**	**9**	**30**	**39**	**38**	**58**	**45**	**61**	**70**	**65**	**78**	**106**	**95**	**103**
Total deceased donors	**248**	**220**	**237**	**273**	**291**	**265**	**276**	**263**	**321**	**320**	**306**	**282**	**315**	**321**	**348**

Notes: DCD Cat I: death on arrival; DCD Cat II: unsuccessful resuscitation; DCD Cat III: awaiting cardiac arrest; DCD Cat IV: cardiac arrest while brain death; DCD Cat V: euthanasia.

Figure 1: Utilized deceased organ donors in Belgium (2003-2017) [4]

Waiting lists

In 2017, 95 patients died waiting for deceased donor organs in Belgium (41 for liver, 32 for kidney, 18 for heart, 9 for lung, and 3 for pancreas transplantation). By December 31, 2017, 1292 patients had been listed for transplantation (849 for kidney, 201 for liver, 143 for lung, 103 for heart, and 61 for pancreas transplantation respectively) [4].

Guidelines for potential donors after brain death

A systematic review of the effects of evidence-based clinical practice guidelines (CPGs) in general on the quality of care showed that they can be effective in improving the process and structure of care [5]. An early definition of CPGs by the Institute of Medicine [6] described these as 'systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances.' This definition was updated in 2011 to put more emphasis on the rigorous methodology in the guideline development processes: 'Clinical guidelines are statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options' [7]. In this rapidly evolving field of research, a more recent definition focused on guideline implementation: 'Guidelines are a convenient way of packaging evidence and presenting recommendations to healthcare decision makers' [8].

Consensus-based CPGs have been developed for the management of a potential donor after brain death [9, 10]. However, guideline developers concluded that there is a lack of scientific evidence on donor management, from which to derive any level I (at least one RCT with proper randomization), II.1 (well-designed cohort or case-control study) or II.2 (time series comparisons or dramatic results from uncontrolled studies) recommendations. Their conclusions and recommendations were mainly based on clinical experience and informed judgment (i.e., expert opinion = level III) [9-11]. Because of the scarcity of experimental research in this field, the benefits or harms of ICU (Intensive Care Unit) strategies for preserving organ function and improving recipient outcomes are equivocal [10]. Moreover, observational studies suggest that after consent for organ donation, up to 20% of organs may lose transplant potential due to suboptimal medical management [12-14]. Further clinical research is consequently needed to investigate the effects of various donor management strategies, but actually clinical trials of novel interventions in organ donation remain especially scarce [15], largely because researchers in this field face unique challenges. Administration of study interventions in organ donors with the need to measure outcomes among organ recipients is scientifically complicated and

leads to practical difficulties. The different health care services across national borders, to which organs can go, are one example. To advance this research field and to address current knowledge gaps, an ongoing Canadian prospective observational study will investigate current practices and evaluate the therapeutic effectiveness of various donor-specific ICU interventions [16].

In addition and again as a general observation beyond the scope of organ donation, despite extensive investments in research and development (as indicated lacking in the field of organ donation), Grimshaw et al. [17] and others note that relevant research findings are not being fully implemented by healthcare systems and are not appropriately used by others in the chain of scientific research [17-21]. The implication from suboptimal levels of research translation is that the return on research investments is also lower than could be potentially achieved [22]. As well, CPGs are not always translated into policy or practice, despite the widespread recognition of their crucial function [23, 24]. This results in a quality gap when there is a difference between the guideline recommendations and the actual performance in daily practice or when there is a large variability in delivered care between health care professionals or teams.

Research on adherence to guidelines for potential donors is actually largely unknown and most studies have focused on brain death diagnosis. Adherence to the American Academy of Neurology (AAN) guidelines for determination of brain death, updated in 2010, proved variable [25, 26]. A study in 91 countries revealed differences in perceptions and practices of brain death diagnosis worldwide. In comparison to AAN criteria, significant between-hospital variability was documented in examinations, apnea testing, necessity and type of ancillary testing, time to brain death declaration, as well as the number and minimal qualifications of physicians required for declaration [27].

Low adherence to clinical guidelines contributes to omission of beneficial therapies, preventable harm, suboptimal patient outcomes or experiences, or waste of resources [28, 29]. Barriers to guideline implementation and adherence can be differentiated into personal factors (e.g. lack of awareness), guideline-related factors (e.g. lack of evidence and the plausibility of recommendations),

and external factors (e.g. organizational constraints) [30]. To improve the development of guidelines, Pronovost described five strategies to increase adherence to clinical guidelines: (1) include an unambiguous checklist with interventions (supported by ranked evidence) linked in time and space in the clinical guideline; (2) help clinicians to identify and mitigate barriers and share successful implementation strategies; (3) collaborate to integrate guidelines for conditions that commonly coexist, (4) rely more on systems than the actions of individuals to ensure that patients receive the recommended care and (5) create transdisciplinary teams and pool expertise from different fields to deliver practice-focused guidelines [28]. To improve the implementation of guidelines, a recent review revealed the following aspects as central elements of successful strategies: dissemination, education and training, social interaction, decision support systems, and standing orders and standardized documentation [30]. These strategies are closely linked to a concept that was introduced in the 1990's named critical pathways, later also known as clinical pathways or care pathways. Whilst broadly similar to CPGs, clinical pathways differ by being more explicit about the sequence, timing and provision of interventions. They are usually based on CPGs and contextualized for use within specific environments or circumstances [31].

Care pathways

One promising method of minimizing the quality gap between scientific evidence and practice is the implementation of care pathways. Care pathways are tools used by healthcare professionals to guide evidence-based practice and improve the interaction between health services. They bring the available evidence to a range of healthcare professionals by adapting guidelines to a local context and detailing the essential steps in the care of patients with a specific clinical problem [32]. The European Pathway Association nowadays defines a care pathway as "a complex intervention for the mutual decision making and organization of care processes for a well-defined group of patients during a well-defined period". Defining characteristics of care pathways include: (I) An explicit statement of the goals and key elements of care based on evidence, best practice,

and patients' expectations and their characteristics; (II) The facilitation of the communication among the team members and with patients and families; (III) The coordination of the care process by coordinating the roles and sequencing the activities of the multidisciplinary care team, patients and their relatives; (IV) The documentation, monitoring, and evaluation of variances and outcomes; and (V) The identification of the appropriate resources. The aim of a care pathway is to enhance the quality of care, across the continuum, by improving risk-adjusted patient outcomes, promoting patient safety, increasing patient satisfaction, and optimizing the use of resources" [33, 34]. While developing and implementing a care pathway, a least 3 active ingredients are necessary: (1) information on a set of evidence-based key interventions, (2) feedback on the actual organization of the care process and (3) training in how to develop, implement, evaluate, and follow-up a care pathway based on the seven-phase methodology [35]. This method includes a screening phase, a project management phase, a diagnostic- and objectification phase, a development phase, an implementation phase, an evaluation phase and a continuous follow-up phase [36]. Evidence exists to support the use of care pathways. Different studies showed that care processes supported by care pathways were better organized and that their implementation has an effect on patient, process, and team outcomes [31, 37-39].

Patient and process outcomes provide data to understand if care pathways work [40]. A Cochrane study, performed by Rotter et al. (2010) concluded that care pathways improve documentation of care and reduce in-hospital complications without a negative impact on length of stay and hospital costs [31]. However, because care pathways are complex or consist of multicomponent interventions we have to be careful in generalizing results. As stated by Vanhaecht et al. (2011), due to different contexts, it could be inappropriate to simply take over implementation strategies from one organization to another. Multidisciplinary teams should therefore invest in the organization of care processes by understanding the development, change, and implementation process in their particular context [41]. In addition, several reviews and meta-analyses found evidence that the implementation of a care pathway leads to higher patient satisfaction [42], reduced hospital costs [42-45] and reduced length of stay [42-48]. However, some reviews found insufficient evidence for

proving differences in postoperative complications [44], postoperative mortality [46, 47], readmission rates [46-48] and hospital costs [48]. In addition, there is variability in and suboptimal inclusion of evidence-based key interventions and quality indicators in the care pathway documents, which can lead to quality and patient safety issues [49-51]. Moreover, there is no conclusive evidence that care pathways lead to more adherence to guidelines. Although different studies found a significantly higher adherence to guidelines [52-54], some studies found no significant impact on guideline adherence [55, 56].

Team outcomes provide data to understand why and how care pathways work [40]. A systematic review revealed that care pathways have the potential to support interprofessional teams in enhancing teamwork. Most frequently positive effects after implementation of a care pathway were found on staff knowledge, interprofessional documentation, team communication and team relationships [57].

In summary, care pathways research has several limitations. First of all, care pathway research is mainly performed in weakly designed studies [58-60]. As complex interventions, care pathways induce change at different levels of the organization (i.e. patient, team, hospital,…). Cluster randomized controlled trials (cRCT) are therefore the gold standard to be used to study the impact of care pathways, but only a few cRCT on pathway effectiveness have been conducted up to the present [35, 40, 56, 61]. One reason for that is the difficulty to randomize multidisciplinary teams into experimental and control groups, as compared to randomization of patients in conventional randomized controlled trials. Therefore, very often a quasi-experimental design, like a pretest-posttest or time series design, is used to evaluate pathway effectiveness [31]. Secondly, because care pathways are primarily developed for high-volume hospital diagnoses and low complexity care processes [62-64], research is limited for several interesting low-volume patient populations, e.g. organ donation. Thirdly, it is difficult to compare the adherence to CPGs and outcomes of different care pathways for a specific pathology, because there is a large variation of the included key interventions and lack of consistency in the measured adherence to CPGs and outcomes [49-51]. Fourthly, the effect of care pathways on guideline adherence in

reducing the variability in clinical practice is not inclusive. Only a few studies have been performed up to now to analyze the impact of care pathways on guideline adherence and to identify the determinants of guideline adherence [52-56].

Importance performance analysis

As stated before, one of the active ingredients before developing and implementing a care pathway, is gathering feedback on the actual organization of the care process to analyze if there is a research-practice gap. This gap can be visualized by an importance-performance analysis (IPA). This tool indicates whether scientific knowledge is not fully used in clinical practice, potentially depriving patients from the highest quality care [17, 65, 66]. This kind of visualization was originally proposed in marketing research and is rather new in healthcare [67, 68]. As shown in Figure 2, the two-dimensional IPA model is divided into four quadrants with performance on the x-axis and importance on the y-axis. As a result of this, four quadrants namely *Concentrate Here*, *Keep up the Good Work*, *Low Priority*, and *Possible Overkill* are created [68]. The importance rate can be identified through (inter)national Delphi study [69] or level of evidence weighting [70]

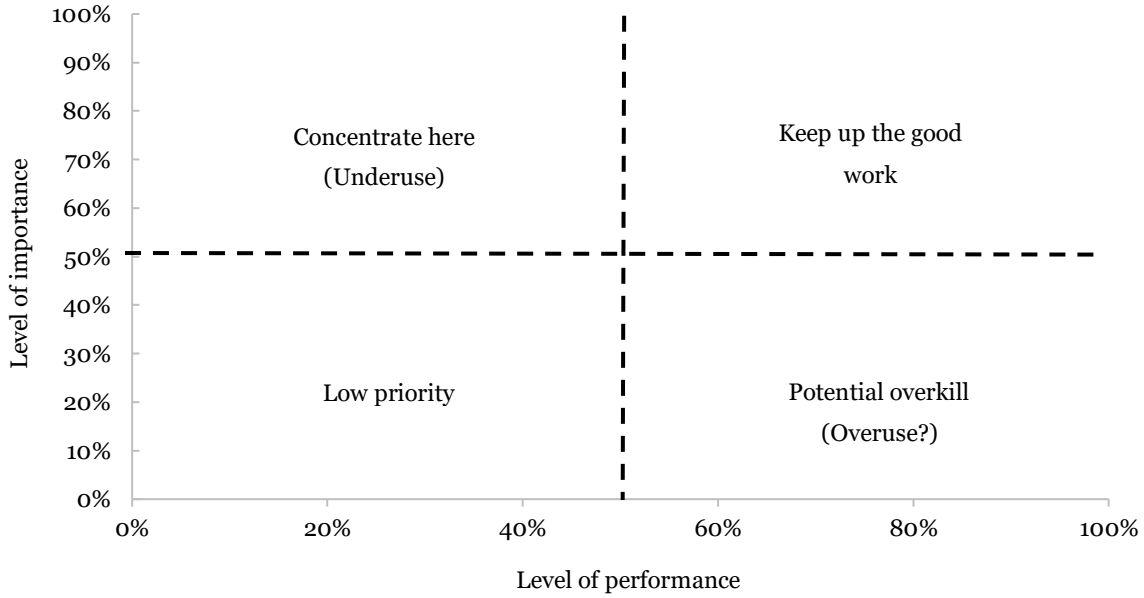


Figure 2: Importance-performance analysis

Some recent IPA studies have been published for patients with colorectal cancer, COPD, hip fractures or STEMI. The same trend was noticed in these patient groups. In general, most care interventions have a low performance rate in spite of high importance rate (underuse care interventions) and only a limited number of care interventions had a high performance but a low importance rate (possible overuse care interventions) [69-72]. Also, for example to improve pediatric health care, it was found to be a good method, because the authors concluded that the attribute importance moderates performance and quality. If the level of attribute importance is not taken into consideration, regardless of the attribute performance, health care organizations may spend valuable resources targeting the wrong areas for improvement [67]. These underuse and possible overuse care interventions should be priorities for hospitals. A series of articles published in The Lancet shows that underuse of proven medical care and overuse of unproven services causes coexist within populations, within systems, and even within patients around the world, causing suffering to millions of people. The costs are serious: physical, psychological, and social harms for patients and wasteful misallocation of resources for society. The authors conclude that the deepest drivers of poor care arise out of fundamental inequalities of information, wealth and power. The path to the right care will therefore require more data on underuse and overuse, a deeper understanding of care delivery as a science, political consensus for redirecting investments towards new, more balanced delivery models, and leadership from clinicians to create an activated, informed and mobilized citizenry [73].

Due to the high number of priorities and actual financial constraints in healthcare policy, there is an urgent need to tackle underuse and overuse together to achieve the right care. An IPA presents a possible approach to set priorities around which to design and implement effective quality improvement initiatives. One of the methods for improving adherence to guideline can be through the use of a care pathway.

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Chapter 2

Aims of this thesis

2. Aims of this thesis

This doctoral thesis examined different research questions regarding the recommended care for potential donors after brain death and adherence to guidelines in this setting in Belgian intensive care units. The aims were (1) to investigate the impact of existing care pathways for donation after brain death on the quality of care, (2) to identify and select a set of relevant key interventions and quality indicators in order to develop a specific care pathway for donation after brain death and to rigorously evaluate its impact, (3) to assess adherence to these key interventions for the management of potential donors after brain death in a perspective of organ donation in Belgian hospital intensive care units and (4) to define recommendations for further improvement of the deceased organ donation process up to organ procurement in Belgium. The next four main research questions (RQs) were addressed in this PhD study.

RQ 1 What is the impact of existing care pathways for donation after brain death on the quality of care according to the literature? (Chapter 3)

RQ 2 Which set of key interventions should be included in a care pathway for donation after brain death? (Chapter 4)

RQ 3 Which quality indicators should be followed up when evaluating the quality of care for potential DBDs and the impact of a care pathway for donation after brain death? (Chapter 4)

RQ 4 What is the adherence to these key interventions for the management of a potential donor after brain death and its association with expert panel ratings of importance? (Chapter 5)

After the introduction, and this chapter, five additional chapters are presented as part of this PhD.

In **Chapter 3** (RQ 1) the results of a systematic review are shown. It reports findings on the effects of existing care pathways for donation after brain death on the quality of care. This chapter discusses the international and local frameworks and more specifically the use and contribution on impact of care pathways for donation after brain death as a tool for improvement.

In **chapter 4** (RQ 2 & 3), it was investigated which relevant key interventions and quality indicators can be identified and selected in order to develop a specific adult care pathway for donation after brain death and to rigorously evaluate its impact. A RAND modified three-round Delphi approach was used to build consensus within Belgium about potential key interventions and quality indicators identified in existing guidelines, review articles, process flow diagrams and the results of the Organ Donation European Quality System (ODEQUS) project.

Chapter 5 (RQ 4) investigated, through a retrospective review of patient records, whether guideline adherence to an expert panel predefined care set in management of a potential donor after brain death would reveal room for improvement. As literature is lacking regarding the guideline adherence rates for potential donors after brain death and to target the right areas for improvement, an important-performance analysis was performed. This analysis is an approach for prioritizing key interventions for improvement, by linking key interventions with expert panel ratings of importance to the performance indicator of guideline adherence rates.

In **chapter 6**, it was investigated by a Belgian expert panel if there are recommendations for further improvement of the deceased organ donation process up to organ procurement in Belgium. Although Belgium has achieved high deceased organ donation rates, deceased potential donors are still missed along the pathway. As such, there remains substantial room for further improvement of the deceased organ donation process and the development and

implementation of a care pathway for donation after brain death is only one of the tools, more specifically to support guideline implementation in donor hospitals. This chapter debates different issues in the monitoring of donation activities, practices and outcomes; donor pool; legislation on deceased organ donation; registration; financial reimbursement; educational and training programs; donor detection and practice clinical guidance.

Finally, in **chapter 7** the main findings, overall discussion and general conclusion of this PhD dissertation are addressed. Furthermore, implications, limitations of the current studies and ideas for future research are discussed.

Chapter 3

Care pathways for organ donation after brain death: guidance from available literature?

Pieter Hoste
Kris Vanhaecht
Patrick Ferdinande
Xavier Rogiers
Kristof Eeckloo
Stijn Blot
Eric Hoste
Dirk Vogelaers
Koenraad Vandewoude

Published in Journal of Advanced Nursing 2016; 72(10): 2369-2380

3. Care pathways for organ donation after brain death: guidance from available literature?

Abstract

Aims. A discussion of the literature concerning the impact of care pathways in the complex and by definition multidisciplinary process of organ donation following brain death.

Background. Enhancing the quality and safety of organs for transplantation has become a central concern for governmental and professional organizations. At the local hospital level, a donor coordinator can use a range of interventions to improve the donation and procurement process. Care pathways have been proven to represent an effective intervention in several settings for optimizing processes and outcomes.

Design. A discussion paper.

Data sources. A systematic review of the Medline, CINAHL, EMBASE and The Cochrane Library databases was conducted for articles published until June 2015, using the keywords donation after brain death and care pathways. Each paper was reviewed to investigate the effects of existing care pathways for donation after brain death. An additional search for unpublished information was conducted.

Discussion. Although literature supports care pathways as an effective intervention in several settings, few studies have explored its use and effectiveness for complex care processes such as donation after brain death.

Implications for nursing. Nurses should be aware of their role in the donation process. Care pathways have the potential to support them, but their effectiveness has been insufficiently explored.

Conclusion. Further research should focus on the development and standardization of the clinical content of a care pathway for donation after brain death and the identification of quality indicators. These should be used in a prospective effectiveness assessment of the proposed pathway.

Summary Statement

Why is this discussion paper needed?

- There is a growing interest in possible strategies to improve the donation process at the hospital level.
- The implementation of a care pathway for organ donation after brain death could be one possible strategy to standardize the donation process and to optimize outcomes.
- The effectiveness of these care pathways has not been critically appraised.

What are the key findings?

- The systematic review revealed a lack of publications that evaluated the effect of care pathways for donation after brain death.
- Care pathways are primarily developed for high-volume hospital diagnoses and low complexity care processes, for which organ donation after brain death does not qualify.
- Care pathways can be an effective tool for improving adherence to guidelines, documentation of donor management goals and communication with relatives, as well as physician agreement about donor treatment options.

How should the findings be used to influence policy/practice/research/education?

- Research on a national level should focus on the development and standardization of the clinical content of a care pathway for donation after brain death, taking into account the specific features of the national health organization.
- A set of quality indicators should be developed to investigate the effectiveness of such a care pathway.

Introduction

The availability of suitable donors and organs is a major limitation for organ transplantation [1, 2]. The majority of transplants originate from donors after brain death. In 2014, 90% (n = 1836) of deceased donors were donors after brain death (DBD) and 10% (n = 205) after circulatory death (DCD) in the Eurotransplant area. Therefore, 6721 transplants came from DBD and 472 transplants from DCD. In addition, the importance of living donation is increasing, particularly for kidney transplantation [3]. The number of organs transplanted per donor (OTPD) is also higher, apart from kidney transplant, from donation after brain death (DBD) donors compared to donation after circulatory death (DCD) donors. In the USA, the OTPD from DBD donors was 3.3 compared with 1.9 OTPD from DCD donors in 2013 [4]. Despite considerable efforts, there remains an imbalance between the number of available organs and potential recipients and a significant variability in practices and approaches to increase donor rates. This paper will discuss the international and local frameworks and more specifically the use and contribution on impact of care pathways for DBD as a tool for improvement.

Background

International framework

International political organizations and professional bodies have responded to the challenges of the worldwide shortage of organs for transplantation, the international variability in donation and transplantation activity as well as the need to provide a firm legal and ethical basis ensuring equity, quality and safety [5]. The international governmental response resulted in revised Guiding Principles on Human Cell, Tissue and Organ Transplantation [6, 7], referring to both living and deceased donation. It articulates the importance of pursuing national or sub-regional self-sufficiency, in particular through increased efforts to promote deceased donation. The professional response to these challenges has been led by The Transplantation Society, in association with other international professional societies, through publications

including the Amsterdam Forum [8], the Vancouver Forum [9] and importantly the Declaration of Istanbul on Organ Trafficking and Transplant Tourism [10]. A further joint initiative between governmental and professional organizations consisted of The Third Global Consultation on Organ Donation and Transplantation organized by the WHO, The Transplantation Society and the Spanish Organización Nacional de Trasplantes, supported by the European Commission. This meeting resulted in the Madrid Resolution [11], calling for a global goal of national responsibility in satisfying organ donation and transplantation needs. This Resolution aims at self-sufficiency at the country level as well as regulated and ethical international cooperation, when needed in the face of insufficient resources. The concept of self-sufficiency does not only stress the necessity to increase organ donation activity but also to decrease actual transplantation needs in a given population.

The task of establishing an adequate capacity management, regulatory control and a suitable normative environment is a national responsibility [11]. Far from achieving this goal, more than 133,000 potential transplant recipients are currently on waiting lists in the UK, USA and Eurotransplant areas [12]. Worldwide there is a large variability between different countries in organ availability, ranging from as low as 2.9 donors per million inhabitants in Russia to 35.3 in Spain in 2013 [13]. Possible explanations include differences in legislation, management, organization of deceased organ recovery programs or education of professionals [1, 5]. Although multifactorial approaches are needed to address the issue on different levels, besides legislative modifications [14], social awareness [15, 16], mass media campaigns [16-18], ethics [19] and religion [20], the availability of professionals specifically trained in organ donation [21-23] and their engagement in the proactive donor detection systems at hospital level [24] are highlighted as major factors by many national and international programs.

Local framework

Analysis of best practice shows that a well-supported, trained donor coordinator in the hospital [25, 26] is key to maximizing deceased donor potential and eventually increasing donation rates. This was also acknowledged by the European Parliament & the Council of the European Union (EU). Beside a physician, nurses can also perform this function. Consequently, the EU published a binding directive on quality and safety standards for human organs used for transplantation in 2010, to be implemented by all Member States in 2012. The role of the donor coordinator was recognized as essential to improving not only the effectiveness of the donation and transplantation process but also the quality and safety of transplantable organs [27].

To improve the donation process at the hospital level, a donor coordinator can use a range of educational (e.g. flyers, workshops or lecture) and/or organizational interventions (e.g. implementing guidelines). A systematic review of Douville *et al.* (2014) shows that, despite the large number of publications, few of these interventions have been evaluated. Evaluation designs suffered from several weaknesses. Only few studies used a comparison group. In addition, methodological flaws (including vague intervention definition, absence of a theoretical framework, lack of explanations on study design or unjustified sample size) hamper firm conclusions on their efficacy. Therefore, they state that interventions should be based on theoretical frameworks and would benefit from more rigorous evaluation methods to ensure a better transfer of knowledge and appropriate organizational decisions [28].

Care pathways

The European Pathway Association defines a care pathway as ‘a complex intervention for the mutual decision-making and organization of care processes for a well-defined group of patients during a well-defined period’ [29]. Several reviews reported positive effects on clinical outcomes, costs, patient satisfaction, teamwork, performance of care processes and risk of burnout in healthcare teams

[30-36]. Care pathways are used worldwide for a variety of patient groups [37-40]. They support the translation of clinical guidelines into local protocols and introduction into clinical practice [37] and support healthcare teams in implementing evidence-based key interventions and reduce clinical variability [38]. A major issue in the management of potential DBD is the variability in care processes and outcomes. One possible strategy to standardize the donation process and to optimize outcomes could be the implementation of a care pathway. However, previous published systematic reviews on pathway effectiveness did not focus on care pathways for DBD. Therefore, the following research question is explored in this discussion paper: 'What is the impact of existing care pathways for DBD on the quality of care?'

Data sources

Search strategy

We performed a systematic review on the effects of existing care pathways for DBD. A sensitive search strategy was carried out in the electronic databases MEDLINE, CINAHL, EMBASE and The Cochrane Library for articles published until June 2015 without limitation by year. However, we only examined the full text of relevant articles in English, German, French, Dutch and Italian. Both Mesh and non-Mesh terms for DBD and care pathways were combined which led to the following Medline search strategy: ('brain death' [Mesh] OR 'donor selection' [Mesh] OR 'tissue and organ harvesting' [Mesh] OR 'tissue and organ procurement' [Mesh] OR 'tissue donors' [Mesh] OR 'brain death' [Text word] OR 'brain dead' [Text word] OR 'donation' [Text word] OR donor* [Text word]) AND ('critical pathways' [Mesh] OR care pathway* [Text word] OR clinical path* [Text word] OR critical path* [Text word] OR integrated care pathway* [Text word] OR care map* [Text word]). The strategy was translated for the other databases. Conference abstracts were excluded. We also performed snowballing through the reference lists of identified publications. When the full text of a relevant article was not found, the authors were contacted for further information. In the absence of the requested information, the article was excluded. Since the literature search in electronic databases revealed a limited amount of papers, we conducted an

additional search for unpublished information in Google, using the search terms brain death, organ donation and critical pathway.

Appraisal for inclusion

Appraisal of the retrieved records occurred in two phases. All retrieved documents were primarily screened on title and abstract by two reviewers (PH and PF). A first selection was based on the description of the study population and the general characteristics of the care pathways. Subsequently, the full texts of the selected articles were independently screened by three researchers (PH, PF and KV) on the inclusion criteria of: (I) implementation and evaluation of care pathways for DBD; (II) original collected data. To qualify as a care pathway, the intervention was evaluated on criteria based on the care pathway definition of the European Pathway Association [41]: (I) aimed at a well-defined group of patients during a well-defined period; (II) an explicit statement of the goals and key elements of care based on evidence, best practice, patients' expectations and their characteristics; (III) coordination of the roles and sequencing of the activities of the multidisciplinary care team, patients and their relatives; (IV) documentation, monitoring and evaluation of variances and outcomes; (V) identification of relevant resources [29]. For all exclusions based on full text, a reason was noted. The first author subjected all studies meeting the inclusion criteria to quality appraisal by the Scottish Intercollegiate Guidelines Network checklists [42]. These quality assessments were discussed by three reviewers (PH, PF and KV) during a consensus meeting.

Data extraction

For the quality appraisal of each study, included after full text screening, the following data were extracted and reported in overview tables by one reviewer (PH) and checked by two reviewers (PF and KV): author and year; setting and studied period; purpose; population and sample; methods; main outcomes and findings; conclusions and quality assessment (Table 1).

Results

This literature search of the electronic databases and additional sources resulted in 568 publications. The results of the search strategy are presented in Figure 1. After exclusion of duplicates and primary screening by two reviewers (PH and PF), 30 articles were selected for full text screening by three researchers (KV, PF and PH).

Of the 30 articles selected for full text screening, 12 publications were identified through the electronic databases. Nine articles were excluded due to not being relevant. Reasons for exclusion included interventions not addressing or not meeting the characteristics of a care pathway, different care populations, lack of outcome description or unavailability of full text (Figure 1). After quality appraisal using the Scottish Intercollegiate Guidelines Network checklists two articles were rejected and only one study was included, in spite of low quality (Table 1).

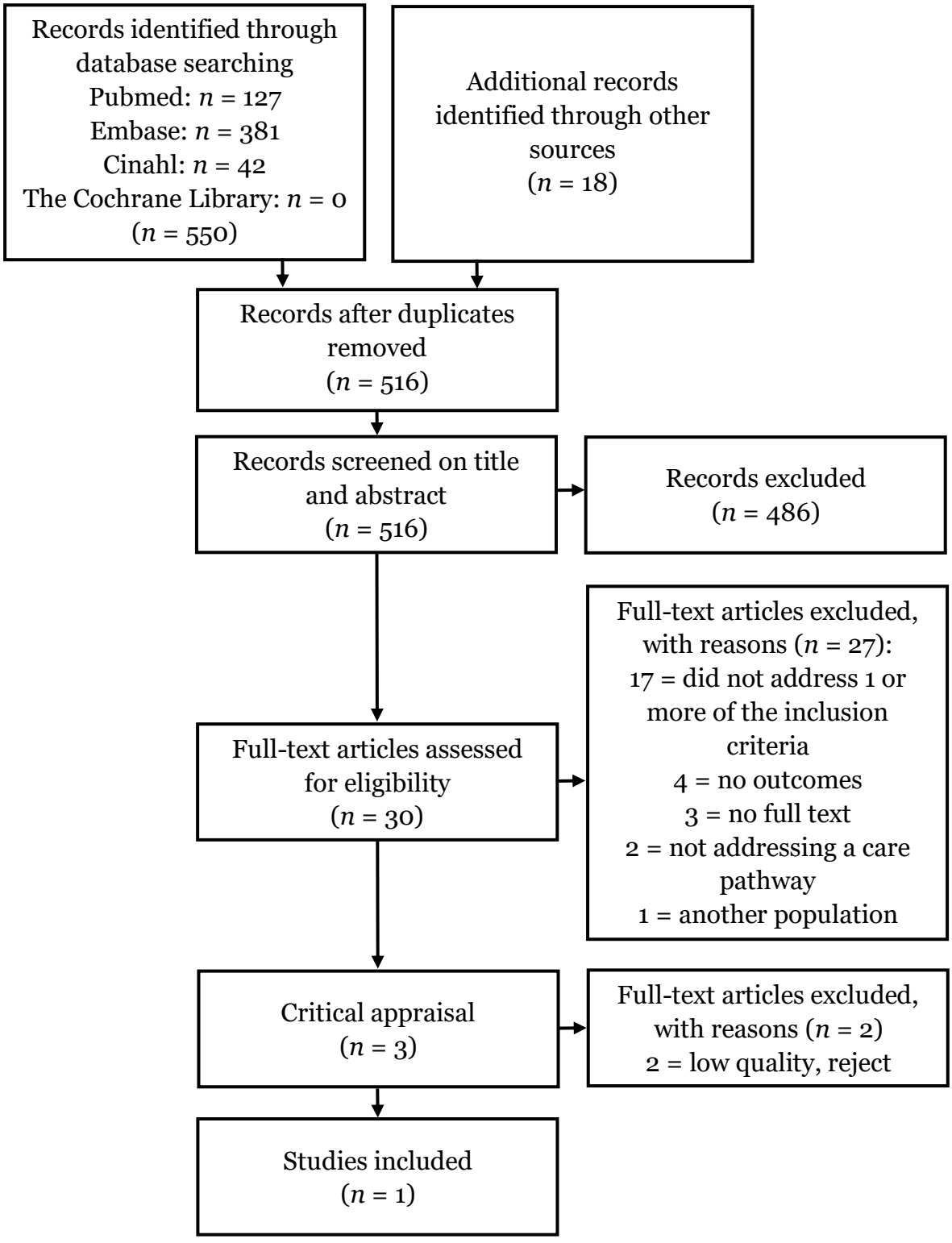

Figure 1: Review stages based on PRISMA flow diagram

Table 1: Studies about the impact of care pathways for donation after brain death

Author and year	Setting and studied period	Purpose	Population and sample
[43]	Setting: University hospital, Norwich, UK Studied period: 2008 - 2010	To review the impact of an embedded specialist nurse in organ donation and the utilization of a collaborative care pathway on potential solid organ donor referrals in an emergency department during a 24-month period.	156401 emergency department attendances. 311 adult patient deaths.
[44]	Setting: University hospital, Ottawa, Canada Studied period: 2001 - 2002	To evaluate the introduction of The Ottawa Hospital's clinical pathway for the multiple organ donor after 1 year.	No description.
[45]	Setting: multicenter (88 critical care units), USA Studied period: 1998 - 1999	To determine the effect of a critical pathway on the donor management and procurement process.	Donors from 88 critical care units in 10 organ procurement organizations. 130 donors were medically managed under the critical pathway, compared with 140 total donors during the control period.

Methods	Main outcomes/findings
Observational study: retrospective cohort design. Referral rates to the organ donation team were compared before and after the introduction of the specialist nurse in organ donation and collaborative care pathway.	Referrals to the organ donation team significantly increased from three of 151 eligible patients (2%) to 26 of 160 patients (16%; Chi-square test; P < 0.0001) following the introduction of a specialist nurse in organ donation into the trust. The number of patients proceeding to organ donation increased from none to two (Fisher's exact test; P = 1.0).
Non-comparative study. Survey of stakeholders.	Use of the pathway has improved the standard of care provided to organ donors and their families. Use of the pathway significantly improves staff's understanding and ability to follow through with the many complex tasks necessary to complete the process.
Experimental study: pre-post test design. Data from the retrospective study were compared with data from the prospective study: demographic information; time of brain death declaration, consent, and cross-clamp of the aorta in surgery; the number and type of organs consented; the number and type of organs actually procured and transplanted; 1-year graft survival; and delayed graft function in the kidneys.	The total number of organs both procured and transplanted per 100 donors was significantly greater (P < 0.01) in the critical pathway group when compared with the control group. There was no significant difference in 1-year graft survival for any of the organs recovered, and no significant difference in the rate of delayed graft function in the kidneys transplanted.

Conclusions	Quality assessment
The presence of an embedded specialist nurse in organ donation in the emergency department and the adoption of a collaborative care pathway to establish clinical triggers for referral to the organ donation team have significantly increased the rate of referral of adult potential organ donors to organ donation services.	Reject
A standardized, integrated and sustained approach to organ and tissue donation has provided improved quality of care not only to potential recipients but also to donor families.	Reject
Use of a critical pathway results in significant increases in organs procured and organs transplanted without any reduction in the quality of the organs being transplanted.	Low quality

The publication of Holmquist *et al.* (1999) described the components of the United Network for Organ Sharing (UNOS) Critical Pathway for the Organ Donor including collaborative practice guidelines, referral of potential donors, declaration of brain death and acquisition of consent from relatives, donor evaluation and management and the surgical recovery of organs. This care pathway provided a multidisciplinary approach to improve communication in the care of donors and incorporated key interventions, multidisciplinary processes and corresponding timelines or phases that health professionals should anticipate in donor care. However, this study did not evaluate the effect of care pathway implementation [46]. This was tested in the study of Rosendale *et al.* (2002), reporting on its pilot introduction in USA in 1999. This study examined brain death donors from 88 intensive care units in 10 organ procurement organizations managed under the critical pathway and compared them to retrospective data collected at the same participating units. The data showed a significant ($P < 0.01$) increase in the number of organs procured (10.3%) and transplanted (11.3%) per donor when compared with an historical control group without any reduction in the quality of the transplanted organs [45]. Results may be limited by the comparison of retrospective data with prospective data because groups may not be comparable. As such, this is the only study to report on the effects of a care pathway in this setting.

The additional search for unpublished information resulted in 18 records which were read in full text and assessed for eligibility. However, all were excluded because of either failure to meet the characteristics of a care pathway or lack of an appropriate study design to address the impact of care pathways on outcomes. Beside the UNOS care pathway [47], in UK, the NICE (National Institute for Health and Clinical Excellence) pathway has been derived from the NICE guideline 'Organ donation for transplantation: improving donor identification and consent rates for deceased organ donation' [48]. In addition, NHS Blood and Transplant has created, in cooperation with Map Of Medicine, clinical pathways for organ donation [49].

Discussion

The systematic review revealed a lack of publications on the effect of care pathways for DBD. This can be explained by the primary development of care pathways for high-volume hospital diagnoses and predictable and low complexity care processes [39, 50, 51]. Literature reveals that care pathways can be effective in supporting proactive care management and ensuring that patients receive relevant clinical interventions and/or assessments in a timely manner for relatively predictable trajectories of care. This may improve service quality and efficiency [50]. The adherence to current guidelines, for example, for brain death determination or donor lung selection, is variable in daily practice [52-54]. Care pathways can be an effective tool for promoting adherence to guidelines or treatment protocols, improving documentation of donor management goals and communication with relatives, as well as improving physician agreement about donor treatment options and supporting decision-making [50].

Care pathways may be less effective in bringing about quality improvements in care processes where services are already based on best evidence and multidisciplinarity is well established. They may need mechanisms to support their implementation and ensure their adoption in practice. In addition, care pathway documentation can introduce new kinds of error [50]. Other studies also raised some concerns about the lack of robust evidence for their development, benefits and effectiveness [38, 55-57], the potential to break down inter-professional boundaries [30, 58] and adverse effects on the individuality of care [57].

Consideration of organ donation should be part of 'end-of-life care'. By implementing a care pathway for DBD, the views and experiences of health professionals on using care pathways for caring for people in the last days to hours of life, should be taken into consideration. The study of Collins *et al.* (2015) revealed the concerns about incorrect use and implementation of the Liverpool End of Life Care Pathway, poor communication with families, junior level staff making decisions and insufficient education and support [59].

The deceased organ donation process can be viewed as a continuum from initial identification of the potential donor to transplantation. Every step can be optimized by a care pathway, including donor identification, brain death determination, donor screening for acceptability of organs, donor management, family approach and authorization or consent for organ donation. Especially in low volume hospitals that are rarely confronted with organ donation a care pathway will facilitate dealing with all these steps [45]. Different studies showed that healthcare professionals fail to recognize potential donors and miss opportunities for organs for transplantation. Therefore a system of defined clinical triggers should be introduced in a care pathway to identify potential suitable donors [60]. The major risks to the recipients are the transmission of infectious or malignant disease with the organ. A care pathway should set out the criteria for screening potential donors and their organs for the risk of disease transmission and potential viability [24].

Appropriate management of the potential donor increases not only the number of organs that can be successfully donated but also has long-term implications for the outcomes of multiple recipients. There has been a shift in the management strategies for the DBD from primarily correcting pathophysiological disturbances associated with brain death, to an algorithmic approach based on achieving clinically relevant end goals to increase the number and quality of transplantable organs [2, 61-63]. Although there is increasing consensus on the appropriate physiological goals, there is significant variability in therapies and techniques used, probably because the optimal combinations of treatment goals, monitoring and treatment techniques have not yet been fully defined [12].

This systematic review demonstrates a lack of evidence on the use of care pathways in spite of their obvious need, adapted to the national context of an individual country. The integration of a set of evidence-based key interventions and outcome, process and structure indicators should be one of the active components in this care pathway [64, 65]. In care pathways for other patient populations, there is variability in and suboptimal inclusion of evidence-based key interventions and quality indicators in the care pathway documents [66-68]. The recently developed and validated eight-step method of Lodewijckx *et al.*

(2012) may facilitate the translation of evidence-based knowledge into key interventions usable for daily practice. These key interventions can overcome barriers and assist professionals both in selecting the best treatment options and in delivering safe and effective care. This eight-step strategy is a time-consuming process, so a team developing a care pathway for DBD should carefully plan an implementation strategy, where sufficient time is provided for proper development of the clinical content [69]. Therefore, we advise to further develop the set of key interventions and quality indicators on a national level and not on a hospital level.

Implications for nursing

Together with physicians, nurses play an important role in the donation care process in an intensive care unit. Both can participate together in the key challenge of detecting and monitoring potential donors and the care for donor relatives. Both nurses and physicians can fill in the donor coordination function at a local hospital. To improve practices regarding the organ donation process they can implement several interventions. But despite the large number of publications about these interventions, only few studies used a control group [28]. This also applies to care pathways for organ donation after brain death. Nurses should be aware that this tool has a potential to improve outcomes but their effectiveness is insufficiently explored.

Conclusion

Care pathways are an effective intervention for improving clinical outcomes, costs, teamwork, performance of care processes and decreasing risk of burnout in healthcare teams, but are lacking in donation after brain death. Further research should focus on the development of such a care pathway, standardizing the complex and less predictable DBD care process and assessment of its effectiveness in low and high-volume hospitals.

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Chapter 4

Development of key interventions and quality indicators for the management of an adult potential donor after brain death: a RAND modified Delphi approach

Pieter Hoste
Eric Hoste
Patrick Ferdinande
Koenraad Vandewoude
Dirk Vogelaers
Ann Van Hecke
Xavier Rogiers
Kristof Eeckloo
Kris Vanhaecht
on behalf of the Donation after Brain Death Study Group

Published in BMC Health Services Research 2018; 18(1):580

4. Development of key interventions and quality indicators for the management of an adult potential donor after brain death: a RAND modified Delphi approach

Abstract

Background

A substantial degree of variability in practices exists amongst donor hospitals regarding the donor detection, determination of brain death, application of donor management techniques or achievement of donor management goals. A possible strategy to standardize the donation process and to optimize outcomes could lie in the implementation of a care pathway. The aim of the study was to identify and select a set of relevant key interventions and quality indicators in order to develop a specific care pathway for donation after brain death and to rigorously evaluate its impact.

Methods

A RAND modified three-round Delphi approach was used to build consensus within a single country about potential key interventions and quality indicators identified in existing guidelines, review articles, process flow diagrams and the results of the Organ Donation European Quality System (ODEQUS) project. Comments and additional key interventions and quality indicators, identified in the first round, were evaluated in the following rounds and a subsequent physical meeting. The study was conducted over a 4-month time period in 2016.

Results

A multidisciplinary panel of 18 Belgian experts with different relevant backgrounds completed the three Delphi rounds. Out of a total of 80 key interventions assessed throughout the Delphi process, 65 were considered to

contribute to the quality of care for the management of a potential donor after brain death; 11 out of 12 quality indicators were validated for relevance and feasibility. Detection of all potential donors after brain death in the intensive care unit and documentation of cause of no donation were rated as the most important quality indicators.

Conclusions

Using a RAND modified Delphi approach, consensus was reached for a set of 65 key interventions and 11 quality indicators for the management of a potential donor after brain death. This set is considered to be applicable in quality improvement programs for the care of potential donors after brain death, while taking into account each country's legislation and regulations regarding organ donation and transplantation.

Background

Organ transplantation has proven to be lifesaving and to have improved the quality of life of numerous patients since the first successful kidney transplant in 1954. As the standard treatment for end-stage organ failure, organ transplantation is currently performed in 112 countries worldwide. In 2015, more than 143,000 patients across the 47 member states of the Council of Europe were on waiting lists for a heart, lung, kidney, liver, pancreas or intestinal transplant. Unfortunately, on average 18 of them died every day because of lack of timely organ availability [1]. The majority of transplant procedures rely on organs from donors after brain death (DBD). DBDs are more likely to donate multiple transplantable organs. The maintenance of perfusion and oxygenation in DBDs creates optimal conditions for successful organ transplantation.

In order to cope with these transplant needs, the field of organ donation and transplantation has been forced to evolve rapidly. Various health care services are required in this complex care process and therefore an effective organization and coordination of all involved health care professionals is essential. Nowadays, in many European Union member states, donor coordinators have been appointed in hospitals with an intensive care unit (ICU), where organ retrieval from deceased donors can be considered. Donor coordinators have clearly defined responsibilities in establishing, managing and reviewing the deceased donation processes in their hospital [2]. To support this, guidelines for the management of potential donors can provide donor coordinators with recommendations based on the best available evidence. However, in spite of efforts to develop standardized guidelines, there remains a large degree of variability in practices amongst hospitals regarding the determination of brain death, application of donor management techniques or achievement of donor management goals [3-7]. These may potentially contribute to under-recruitment of potential organ donors.

A possible strategy to standardize the donation process and to optimize outcomes could lie in the implementation of a validated care pathway. Care pathways are defined by the European Pathway Association as ‘a complex intervention for the mutual decision making and organization of care processes

for a well-defined group of patients during a well-defined period' [8]. They support the translation of clinical guidelines into local protocols and introduction into clinical practice [9]. Care pathways are used worldwide for a variety of patient groups to reduce undesired variability and standardize care based on the latest evidence [10]. They have also been developed for donation after brain death, such as the pathways of the United Network for Organ Sharing, National Institute for Health and Clinical Excellence or National Health Service Blood and Transplant [11-13]. However, a recent systematic review on the effects of existing care pathways for donation after brain death revealed that only one study effectively evaluated the impact of such a care pathway [14].

Typical active ingredients of a care pathway include the promotion of interdisciplinary teamwork, the integration of a set of evidence-based key interventions (KI), and the active follow-up of care processes by a set of quality indicators (QI) to verify compliance to KIs [15]. KIs are those which are required to guarantee high quality care, and hence in this setting will have a significant impact on patient, donor family, recipient or graft outcomes.

The present study therefore aims at selecting a set of KIs to be included in a care pathway for donation after brain death as well as a set of QIs that are relevant to assess the quality of care for potential DBDs and the impact of such a care pathway.

Methods

Study design

To develop a set of relevant KIs and QIs, a RAND modified Delphi technique [16] was used with a predefined number of rounds to stop the Delphi process and a threshold value for consensus [17]. After selection of an extensive set of KIs and QIs from the literature and composition of a multidisciplinary expert panel, three anonymous questionnaire rounds and one physical meeting were performed to achieve panel consensus about the relevance of the proposed KIs and relevance and feasibility of the proposed QIs. Questionnaires were conducted through

LimeSurvey®, an open-source software tool to conduct online surveys [18]. E-mail reminders were sent at 2 weeks following the initial email of each round. The consensus procedure took place between March and June 2016.

Composition of expert panel

The objective was to generate a multidisciplinary Delphi panel of physicians and nurses involved in the donation process after brain death in Belgium in order to guarantee relevance for clinical practice and generalizability of results [17, 19]. The main eligibility criteria consisted of a longstanding experience in the field of organ donation, preferably for a minimum of 10 years, and a minimum of 3 organ donors throughout 2015 in the donor hospital, in which the expert was professionally active.

All Belgian donor coordinators (n = 196), the board members of the Belgian Society of Intensive Care Medicine (n = 8), and the members of the Transplant Coordinators Section (n = 28) and the Belgian Organ Procurement Committee (n = 19) of the Belgian Transplantation Society were invited to join this study by an information letter (Additional file in Chapter 10) sent by e-mail by the first author (PH), describing the criteria required to be involved in this Delphi panel.

Selection of key interventions and quality indicators

The selection of KIs and QIs consisted of 8 steps: (1) Delphi questionnaire preparation with extraction of KIs and QIs, (2) first Delphi round, (3) data analysis of the first round, (4) second Delphi round, (5) data analysis of the second round, (6) third Delphi round, (7) data analysis of the third round, and (8) physical consensus meeting.

- Step 1: Delphi questionnaire preparation with extraction of key interventions and quality indicators

To develop a Delphi questionnaire including all possible relevant and feasible KIs and QIs, an extensive literature review was conducted by the first author (PH). For the review of guidelines on the management of a potential DBD, the following resources were explored: (I) Websites of national European transplantation organizations or societies: Agence de la biomédecine, British Transplantation Society, Deutsche Stiftung Organtransplantation, Nederlandse Transplantatie Stichting, NHS Blood and Transplant, and Organización Nacional de Trasplantes; (II) Websites of European transplantation or intensive care medicine organizations or societies: European Directorate for the Quality of Medicines and HealthCare, European Society of Intensive Care Medicine, European Society of Organ Transplantation, Eurotransplant, and Scandiatransplant; (III) Websites of international transplantation societies: International Liver Transplantation Society, International Transplant Nurses Society, The International Society for Heart & Lung Transplantation, and The Transplantation Society; (IV) Public resources for evidence-based clinical practice guidelines: Guidelines International Network, National Guideline Clearinghouse, National Institute for Health and Clinical Excellence, and Scottish Intercollegiate Guidelines Network; (V) Process flow diagrams based on evidence-based medicine: Map of Medicine and National Institute for Health and Clinical Excellence; and (VI) Electronic databases: MEDLINE, CINAHL and EMBASE.

For the first 5 resources, the following search terms were used: 'organ donation' and 'brain death'. For the electronic database MEDLINE, the Medical Subject Headings (MeSH) terms 'brain death', 'donor selection', 'tissue and organ harvesting', 'tissue and organ procurement' or 'tissue donors' were used in combination with 'guideline' or 'practice guideline', both as publication type. The strategy was translated for the other databases. Search limit parameters included: (I) published between 2009 and 2015, and (II) written in English, Dutch or French.

Only few of these guidelines included KIs for donor management [20-22]. Therefore, an additional search was performed in the electronic databases, MEDLINE, CINAHL, EMBASE and The Cochrane Library, to include recent review articles, using the search term 'donor management'. In addition to the QIs listed in the guidelines and review articles, the QIs identified in the organ donation process of the Organ Donation European Quality System (ODEQUS) project were also analyzed. These were developed by a consortium involving associated and collaborating partners from 16 European countries [23].

A two-phase screening evaluation of publications from these resources was applied. In the first phase, publications were appraised for relevance based on appropriateness of the title and abstract. If relevance was unclear, or if the abstract was unavailable, the full text of these publications was assessed. In the second phase, the full text of the selected guidelines or process flow diagrams were reviewed. Following inclusion criteria were applied: (I) descriptions of KIs or QIs regarding an adult patient with a devastating brain injury or lesion with evolution to imminent brain death until post procurement, and (II) underpinning by in-text references of evidence to support their practice. The guidelines selected after full text review were appraised using the validated AGREE II-Global Rating Scale (AGREE II-GRS) quality assurance tool for clinical practice guidelines. This instrument consists of 4 items assessing the quality of guideline reporting. Each item is scored on a seven-point scale [24]. Guideline quality was independently rated by three reviewers (PH, KV and PF). A consensus meeting was held between these reviewers to determine the mean score of the overall guideline quality. Disagreements between reviewers during quality rating were resolved through discussion until consensus was reached. Only clinical practice guidelines with a mean score of 5-7 points on the overall guideline quality were included.

After the extensive literature review, potential KIs and QIs were selected by PH, EH and PF. These KIs and QIs were integrated in an internet-based Delphi questionnaire, consisting of three main parts: demographic questions (name and type of hospital or organization, number of intensive care beds, number of organ donors, professional group, function, years of experience in organ donation, age and gender), KIs and QIs. The demographic questions are included in the

Additional file in Chapter 10. The provisional Delphi questionnaire was pretested by three intensivists, who were not eligible to participate in the expert panel.

- Step 2: Delphi round 1

During the first round, the participants received an e-mail with a link to the internet-based Delphi questionnaire. In addition to the demographic information, experts were asked to provide comments on the listed KIs and QIs or add new ones.

- Step 3: data analysis of Delphi round 1

Based on the comments in Delphi round 1, adjustments with regard to the description of the KIs and QIs were made and KIs or QIs were deleted. Newly identified KIs or QIs suggested by the expert panel were included in the questionnaire.

- Step 4: Delphi round 2

In preparation for the second round, the participants received feedback of all the first-round panel members' comments, deleted KIs and QIs, and the additionally proposed KIs and QIs. In the first part of the second Delphi round, experts were asked to rate on a 9-point Likert rating scale (score 1 indicating "strongly disagree"; score 9 "strongly agree"), to what extent each KI would contribute to the quality of care for the management of a potential donor (or the donor family, recipient or graft) and similarly to which extent each QI could be considered relevant and/or feasible to be implemented. The KIs & QIs of the Delphi round 2 are presented in the Additional file in Chapter 10.

- Step 5: data analysis of Delphi round 2

The results of the second round were analyzed using predefined consensus criteria based on a systematic review about the use and reporting of the Delphi method for selecting health care QIs [17]. A KI was considered valid if it had a median score of 7 or more with 75% or more of the ratings in the highest tertile (Likert score: 7-9). A QI was accepted with agreement if the attribute relevance had a median score of 7 or more with 75% or more of the ratings in the highest tertile (Likert score: 7-9) and the attribute feasibility had a median score of 7 or more.

- Step 6: Delphi round 3

In round 3, feedback on the quantitative panel results was provided to all members of the panel, presented by the following summary statistics: central tendencies (median, minimum, maximum, and mode), frequency of ratings in each tertile Likert category (1-3, 4-6, and 7-9), rating of contribution (ratio of "sum of ratings on the intervention given by participants" to "sum of ratings on the intervention if all respondents rated the interventions as 'strongly agree'"), and the respondent's own responses. Using this information, respondents were asked to re-rate the KIs and QIs in case they would like to change their previous answers.

- Step 7: data analysis of Delphi round 3

The same predefined consensus criteria as in step 5 were applied to the analysis of the results of the third Delphi round. If participants of round 2 did not respond in round 3, their answers of round 2 were considered as final.

- Step 8: physical consensus meeting

A face-to-face consensus meeting (June 2016) was organized to discuss and re-rate the KIs and QIs without consensus after the third round [17]. The nominal group technique was used as consensus method [25]. One author (DV) moderated this meeting in order to contain the influence of dominant personalities. Another author (PH) presented the available literature concerning the 'no consensus' KIs and QIs. Subsequently, the experts had the possibility to discuss the literature, followed by the opportunity for re-rating previous individual scores using the same Likert rating scale.

Results

Delphi panel participants' characteristics

A total number of 20 eligible experts agreed to participate in this study. The expert panel had an average of 18-year experience in the field of organ donation (Table 1 for more detailed characteristics of the expert panel). In round 1, 18 of 20 invited experts completed the questionnaire. All 18 participants completed the three Delphi rounds. The physical meeting was attended by 9 experts.

Table 1: Characteristics of the Delphi panel (n = 18)

Characteristics	**n (%)**
Gender	
Male	9 (50)
Female	9 (50)
Age (years)	
30-49	7 (39)
50-69	11 (61)
Professional group	
Medical doctor	11 (61)
Nurse	6 (33)
Other	1 (6)

Functions	
Intensive care medicine	11 (33)
Anesthesiology	2 (6)
Intensive care nursing	4 (12)
Donor coordination	13 (39)
Transplant coordination	3 (9)
Years of experience	
5-9	2 (11)
10-19	7 (39)
20-29	9 (50)
Number of organ donors after brain death and circulatory death in 2015	
3-5	4 (22)
6-9	5 (28)
10-25	9 (50)
Type of institution	
Academic hospital	12 (67)
Non-academic community hospital	6 (33)

Development of Delphi questionnaire

The literature research initially revealed 12 guidelines, 9 process flow diagrams, and 1719 digital records from the electronic medical databases. After screening and assessment for eligibility and quality appraisal of full-texts, 10 guidelines [20-22, 26-32] and 9 process flow diagrams [33-41] were included (Figure 1). In addition, several review articles [42-49] and the results of the ODEQUS project [23] were also included.

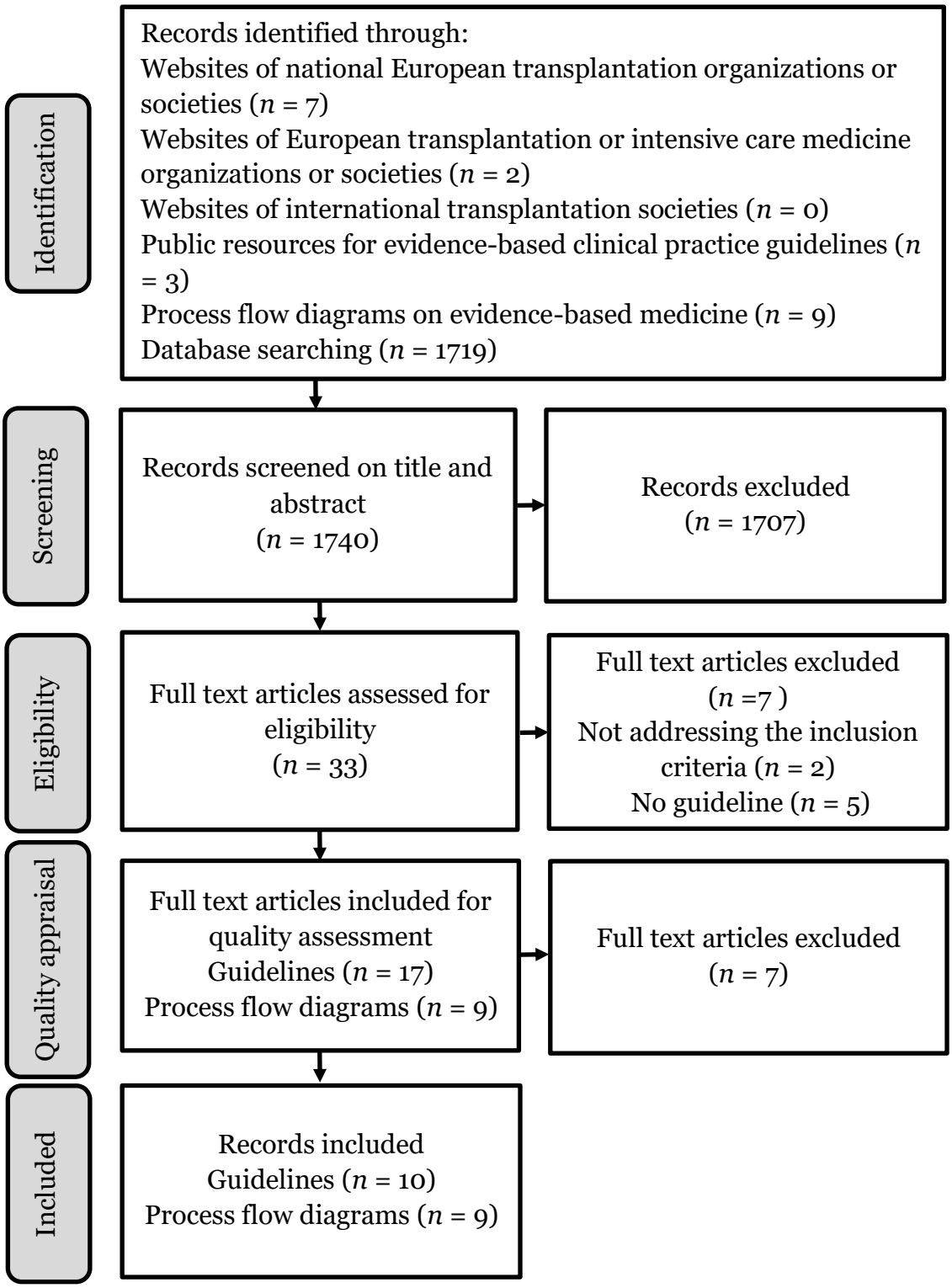

Figure 1: Selection of guidelines and process flow diagrams

Based on the review of the literature, 77 potential KIs and 12 QIs were selected by PH, EH and PF. The KIs were distributed into 10 domains: (I) detection outside the ICU and communication to the ICU (*n* = 1); (II) detection

inside the ICU and notification to a transplant center (n = 12); (III) donor evaluation and characterization (n = 15); donor management: (IV) general care (n = 7), (V) monitoring (n = 20), (VI) cardiovascular management (n = 5), (VII) respiratory management (n = 6), (VIII) renal and electrolyte management (n = 5), (IX) hormone substitution (n = 3); and (X) post procurement care (n = 3). The QIs were distributed into 3 domains: (I) structure (n = 5), (II) process (n = 5), and (III) outcome indicators (n = 2) respectively.

Results of the key interventions

Based on the comments in Delphi round 1, some adjustments with regard to the description of some of the 77 KIs were made and 2 KIs were deleted: '*request to a transplant center to perform a liver biopsy in case of hepatic steatosis and ship it to a transplant center for evaluation by a pathologist*' (donor evaluation and characterization) and '*central venous pressure monitoring, which is used as a dynamic measure to assess volume status or fluid responsiveness*' (donor management: monitoring). There were 5 newly identified KIs suggested by the expert panel, presented in Table 2 and Additional tables. These additional interventions were situated within the topics: 'donor evaluation and characterization', 'donor management: cardiovascular management and hormone substitution', and 'post procurement'.

In the second and third round, the experts could rate the now 80 KIs. The full Delphi panel of 18 experts reached consensus for 65 of the 80 KIs after the third round (data given in Table 2 with their respective Likert ratings). These interventions were considered to contribute to the quality of care for the management of a potential donor (or the donor family, recipient or graft). Because not all the experts could attend the physical meeting after round 3, the results about these 65 KIs with Likert weighted consensus were considered as the final results of this Delphi survey.

Table 2: Results of the 65 key interventions for which consensus was reached by the overall panel after the third Delphi round

	Based on literature (L) or expert panel (E)	Median	Tertile 7-9 (%)	Tertile 7-9 (n)	Rating of contribution (%)*
Detection outside the ICU & communication to the ICU					
Detection of a patient with a devastating brain injury or lesion with evolution to imminent brain death (for example intracranial hemorrhage, trauma, cerebral ischemia etc.) on a unit outside the ICU (for example emergency services, stroke units, etc.) and early communication of the presence of this patient to the ICU physician (and referral to the ICU).	L	8	89%	16	87%
Detection inside the ICU & notification to a transplant center					
Detection of a potential donor after brain death inside the ICU. Detection should be based on defined clinical triggers in patients who have had a devastating brain injury or lesion, while recognizing that clinical situations vary - A Glasgow Coma Scale score of 4 or less that is not explained by sedation and - The absence of one or more cranial nerve reflexes Unless there is a clear reason why the above clinical triggers are not met and/or a decision has been made to perform brainstem death tests, whichever is the earlier.	L	9	100%	18	94%
Notification of the donor coordinator at the time these criteria are met.	L	9	94%	17	91%
Assessment of the prerequisites prior to the clinical evaluation of brain death: - Coma, irreversible, and cause known. - Neuroimaging compatible with coma. - Central nervous system depressant drug effect absent (if indicated, toxicology screen; if barbiturates given, serum level < 10 µg/mL).	L	8	89%	16	83%

- No evidence of residual paralytics (electrical stimulation if paralytics used). - Absence of severe acid-base, electrolyte, and endocrine abnormality. - Normothermia or mild hypothermia (core temperature > 36°C). - Systolic blood pressure > 100 mm Hg. Vasopressors may be required. - No spontaneous respiration.					
Approaching the family: - Delivering bad news about the hopeless, medical situation. - Support of the family (physician, nurse, social assistant, psychologist, pastoral service…).	L	9	100%	18	93%
Notification of the potential donor after brain death by an ICU physician to a transplant center: - Briefing: name, date of birth, diagnosis & therapy, short medical and behavioral history, etc. - Check the medical contra-indications for organ and tissue donation on file with the transplant center. - Is there a registration in the National Register, checked by the transplant center?	L	9	89%	16	91%
Determination of brain death.	L	9	100%	18	95%
Legal declaration of death: registration of time of death and the way in which it is determined on a dated and signed official report.	L	9	89%	16	93%
Notification of legal authorities if the cause of death is unknown or suspicious.	L	9	89%	16	90%
Informing the family about the diagnosis of brain death.	L	9	100%	18	98%
Informing the family about the outcome of the National Register and the possibility of organ and tissue donation, preferably in a separated conversation after family understand and accept the diagnosis of brain death.	L	9	94%	17	94%
Give clear, unambiguous information about the next main steps about the donation	L	9	100%	18	96%

process to the relatives.					
Feedback about the approach of the family and legal authorities (if the cause of death is unknown or suspicious) and discussion about the necessary investigations for donor evaluation and characterization to a transplant center.	L	9	89%	16	90%
Donor evaluation and characterization					
Interviewing family and/or other relevant sources (e.g. life partner, cohabitant, caretaker, friend or primary care physician) to obtain the medical and behavioral history of the potential donor which might affect the suitability of the organs for transplantation and imply the risk of disease transmission.	L	8	89%	16	89%
Reviewing medical charts to obtain the medical and behavioral history of the potential donor which might affect the suitability of the organs for transplantation and imply the risk of disease transmission.	L	9	89%	16	93%
Clinical examination of the potential donor.	L	9	89%	16	91%
Collect a blood sample and ship it to a transplant center for appropriate blood tests.	L	9	100%	18	93%
Discuss with a transplant center, the necessity to examine a blood sample for the determination of ABO, rhesus blood group or additional laboratory tests.	L	9	83%	15	90%
Collect a urine sample (if not shipped to a transplant center) for measurement of sediment, protein & glucose.	L	9	83%	15	87%
Perform a chest X-ray, mandatory for each potential donor and to allow evaluation of a potential lung and/or heart donor.	L	9	89%	16	90%
Discuss with a transplant center, the necessity to perform a bronchoscopy by an experienced physician to allow evaluation of a potential lung donor together with a bilateral bronchoalveolar lavage to collect samples for microbiological tests and to clear mucous plugs or blood clots that may contribute to impaired oxygenation.	L	8	78%	14	81%
Perform an arterial blood gas to allow evaluation of a potential lung donor.	L	9	83%	15	88%

Discuss with a transplant center, the necessity to perform an arterial blood gas for a potential lung donor after 10 minutes ventilation with FiO_2 100% & 5 cm H_2O PEEP.	L	9	83%	15	89%
Perform a 12 lead ECG to allow evaluation of a potential heart donor.	L	9	89%	16	90%
Discuss with a transplant center, the necessity to perform a cardiac ultrasound by an experienced physician to allow evaluation of a potential heart donor.	L	9	89%	16	89%
Discuss with a transplant center, the necessity to perform, if possible, a coronary angiography if cardiac ultrasound is acceptable but other comorbidities are present.	E	8	89%	16	86%
Discuss with a transplant center, the necessity to perform an abdominal ultrasound (or CT scan) to allow evaluation of a potential liver, pancreas and/or kidney donor.	L	8	94%	17	88%
Collect the minimum data, as requested by the transplant center for the characterization of organs and donor, on a donor information form and send it together with the results of the investigations to a transplant center.	L	9	100%	18	93%
Donor management: general care					
Provide at least an arterial line and a central venous line, if not present.	L	8	83%	15	86%
Continue appropriate antibiotic therapy and other life supporting pharmacotherapy, only if indicated.	L	8	94%	17	90%
Use warming mattress, blankets or warmed intravenous fluids if needed, to prophylactically prevent hypothermia.	L	8	78%	14	84%
Reduce vasopressors (if possible) while maintaining hemodynamic stability.	L	9	100%	18	92%
Donor management: monitoring					
Monitor the core body temperature. Target temperature: between 35-37°C.	L	8	100%	18	91%
ECG monitoring of heart rate. Target heart rate between 60-100 beats per	L	8	78%	14	83%

minute.					
Repeat a 12-lead ECG for a potential heart donor if there are subsequent changes in monitored complexes.	L	8	83%	15	87%
Invasive arterial pressure monitoring. Target mean arterial pressure: ≥ 60 mm Hg.	L	9	94%	17	91%
Ensuring a recent chest X-ray examination for a potential lung and/or heart donor is available.	L	9	89%	16	90%
Monitoring of ventilator parameters.	L	9	94%	17	91%
Peripheral oxygen saturation monitoring (SaO_2). Target SaO_2: > 95 %.	L	9	83%	15	91%
Perform a blood gas analysis on a regular basis. Target pH: 7.3-7.5. Target arterial oxygen tension (PaO_2): 80-100 mm Hg. Target arterial carbon dioxide tension ($PaCO_2$): 35-45 mm Hg.	L	8	89%	16	88%
Send a bronchial secretion sample for microscopy and culture if secretions are present.	L	8	89%	16	89%
Perform a bronchoscopy for diagnosis or therapy if clinically indicated.	L	8	83%	15	88%
Estimate the effective intravascular volume and overall fluid status by chart review and clinical examination.	L	8	78%	14	81%
Monitor hourly urine output, particularly looking for any suggestion of the onset of diabetes insipidus (polyuria). Target urine output: 0.5-3 mL/kg/h.	L	8	89%	16	90%
Measure blood electrolytes on a regular basis. Target serum sodium: ≤ 155 mEq/L.	L	8	89%	16	87%
Measure routine full blood counts to examine the need for transfusion of red blood cells if clinically indicated. Target hemoglobin: > 7 g/dL.	L	8	78%	14	81%

Donor management: cardiovascular management (hypotension)					
Use isotonic crystalloids for intravascular volume replacement and use blood products and colloids (albumin) for specific circumstances.	L	8	94%	17	90%
Ensuring an appropriate prescription of vasoactive drugs when correction of the volume deficit fails to achieve the threshold hemodynamic goals.	L	9	100%	18	92%
Donor management: cardiovascular management (bradycardia)					
Treat bradycardia causing hemodynamic instability, with a short acting β-adrenergic agonist (epinephrine/dopamine/dobutamine/isoprenaline) or occasionally transvenous pacing. Don't use atropine because bradycardia are the consequence of high-level vagal stimulation and exhibit a high degree of resistance to atropine.	L	7	83%	15	81%
Donor management: cardiovascular management (tachycardia)					
Treat tachycardia by following the established advanced cardiopulmonary life support guidelines.	E	8	89%	16	87%
Donor management: respiratory management					
Ensuring a lung protective ventilation is installed: - Minimum FiO_2 to obtain a PO_2 between 80-100 mm Hg - Tidal volume (Vt): 6-8 mL/kg (ideal body weight) - Plateau pressure: < 30 cm H_2O - PEEP (Positive End Expiratory Pressure): 8-10 cm H_2O	L	8	89%	16	85%
Maintain 30-45° head of bed elevation to avoid aspiration.	L	8	89%	16	89%
Perform recruitment maneuvers and repeat when indicated.	L	8	83%	15	85%
Apply a prescription of oral hygiene every 6 hours.	L	7	89%	16	84%
Donor management: renal and electrolyte management (oliguria < 0.5 mL/kg/h)					
Treat hypovolemia, hypotension and cardiac dysfunction and consider diuretic only if	L	9	100%	18	93%

needed.

Donor management: renal and electrolyte management (polyuria > 3 mL/kg/h)					
Review the medical history, urinary and blood sample to exclude secondary polyuria: osmotic (Mannitol, hyperglycemia), induced (diuretic) or adapted (fluid overload).	L	8	100%	18	90%
Confirm diabetes insipidus: urine specific gravity below 1.005 g/mL or trend towards hypernatremia/hyperosmolarity.	L	8	94%	17	87%
Treat diabetes insipidus with sufficient fluid volume replacement to compensate polyuria and anti-diuretic hormone replacement. - Fluid volume replacement with monitoring of electrolytes and blood glucose levels. - Anti-diuretic hormone replacement with desmopressin as a first line medication.	L	8	100%	18	93%
Donor management: renal and electrolyte management (electrolyte disturbances)					
Treat electrolyte disturbances.	L	9	100%	18	93%
Donor management: hormone substitution					
Ensuring an appropriate prescription of insulin if treating hyperglycemia to achieve a target glucose level of 180 mg/dL or less.	L	8	83%	15	87%
Post procurement care					
Detection, registration and reporting of serious adverse events to the transplant center.	L	9	100%	18	94%
Debriefing by the donor coordinator and/or transplant coordinator about the results of the transplantation (anonymous) to the relatives, health care professionals and primary care physician.	L	9	94%	17	93%
Offering, if necessary, support to the relatives, for example by a feedback conversation after a couple of weeks or information about associations for relatives.	E	9	94%	17	93%
Debriefing with the involved health care professionals and transplant coordinator.	E	9	89%	16	90%
Ensuring the hospitalization invoice of the patient is excluded of any medical,	L	9	94%	17	94%

pharmaceutical or hospital costs after the determination of brain death and legal declaration of death.	

*rating of contribution = ratio of "sum of ratings on the intervention given by participants" to "sum of ratings on the intervention if all respondents rated the interventions as 'strongly agree'".

The 15 KIs without consensus after the third round are displayed in the Additional tables. In the physical meeting, after discussion of the literature, 9 experts reached consensus about 4 out of the remaining 15 KIs without consensus after the third round: (I) *Continue an appropriate prescription of deep venous thrombosis prophylaxis: low molecular weight heparin* (donor management: general care); (II) *Periodically re-assess cuff pressure to check if there is no cuff leak and if cuff pressure is between 20-30 cm H_2O to avoid aspiration*; (III) *Ensuring coagulation screening or thromboelastography to target therapy if there is a clinically relevant bleeding*; and (IV) *Monitoring of glycemic status to target blood glucose ≤ 180 mg/dL* (donor management: monitoring). The main reasons for not selecting certain KIs after the third round and physical meeting, as described by the experts, were low level of evidence, the prior inclusion in standard ICU care, conflicting evidence, or rather qualification as an additional intervention rather than a KI.

Results of the quality indicators

The expert panel did not suggest new QIs or adjustments to the 12 QIs in the first Delphi round. The full Delphi panel of 18 experts reached consensus for 11 of 12 QIs (4 structure, 5 process and 2 outcome indicators) after the third round. In parallel with the KIs, the results about these 11 QIs with Likert weighted consensus were considered as the final results of the Delphi survey (Table 3).

Table 3: Results of the 11 quality indicators for which consensus was reached by the overall panel after the third Delphi round

	Attribute	Median	Tertile 7-9 (%)	Tertile 7-9 (n)
Structure indicators				
1. Existence of donation process procedures.	Relevance	9	89%	16
Formula: existence of procedures for all relevant steps of the donation process?	Feasibility	9	83%	15
2. Existence of a proactive donor detection protocol.	Relevance	9	89%	16
Formula: existence of a donor detection protocol?	Feasibility	8	72%	13
3. Documentation of key interventions of the donation process.	Relevance	8	89%	16
Formula: existence of a documentation form with all relevant key interventions of the donation process?	Feasibility	8	83%	15
4. Seminars on organ donation.	Relevance	8	83%	15
Formula: number of organ donation seminars organized last year?	Feasibility	8	78%	14
Process indicators				
5. Detection of all potential donors after brain death in the ICU.	Relevance	9	94%	17
Formula: number of potential donors after brain death in the ICU who are referred to the donor coordinator / number of potential donors after brain death in the ICU.	Feasibility	8	83%	15
6. Evaluation of donors after brain death.	Relevance	9	89%	16
Formula: number of patients declared brain death in the ICU who have been evaluated as donors in consult with a transplant center / number of patients declared brain death in the ICU.	Feasibility	8	78%	14
7. Donor management goals.	Relevance	8	83%	15
Formula: number of actual donors after brain death in the ICU meeting 5 of the 7 donor management goals prior to organ recovery (mean arterial pressure: 60-110 mm Hg, number of vasopressors ≤ 1,	Feasibility	8	72%	13

arterial blood gas pH: 7.3-7.5, serum sodium: 135-155 mEq/L, blood glucose: ≤ 180 mg/dL, urine output: ≥ 0.5 mL/kg/h over 4 hours, core body temperature: 35-37°C) / number of actual donors after brain death in the ICU.					
8. Documentation of cause of no donation.	Relevance	9	94%	17
Formula: number of failed potential donors in which the cause of no donation is properly documented / number of failed potential donors.	Feasibility	8	83%	15
9. Documentation of evaluation of potential donors.	Relevance	8	83%	15
Formula: number of donors correctly evaluated / number of donors evaluated.	Feasibility	8	67%	12
Outcome indicators				
10. Family objection to organ donation.	Relevance	9	89%	16
Formula: number of objections (number of potential donor after brain death cases with family objection to organ donation) / number of families interviewed (number of potential donor after brain death cases in which family members are informed about the possibility of organ donation). *exclusion of donor cases where the patient's wishes are known (formal or informal).*	Feasibility	8	78%	14
11. Conversion rate in donors after brain death.	Relevance	9	78%	14
Formula: number of actual donors after brain death / number of eligible donors after brain death.	Feasibility	9	78%	14

The QI without consensus after the third round is included in the Additional tables and was not withheld in the physical meeting.

Discussion

To our knowledge, this is the first report on the selection of a set of KIs that can be used for the clinical content of a care pathway for donation after brain death. A set of 65 KIs was developed as relevant to quality of care. These interventions cover the complete organ donation pathway, including donor detection, brain death determination, family approach, donor evaluation and characterization, donor management, and the post procurement phase. Furthermore, to assess the quality of care for potential DBDs and the impact of this care pathway, a set of 11 QIs was validated for the attributes relevance and feasibility. To include recent data of studies, a continuous monitoring and updating process of this set of KIs and QIs and the resulting donor pathway is obviously needed.

While several guidelines, review articles, and process flow diagrams for the management of a potential donor have been published, there remains a lack of high quality evidence to guide clinical practice. The recommendations are largely based on physiological rationale on the one hand and, consensus statements that overwhelmingly comprised observational studies and retrospective case series on the other hand. This represents low-quality evidence, with a lack of randomized controlled trials [42, 46]. Remarkably however, only 15 of the 80 KIs after the third Delphi round were considered as not valid nor relevant by the expert panel, so consensus was reached for most interventions. This implies that the KIs selected out of the literature are reasonably well in agreement with the opinions of our expert panel, representing a “mainstream” of expert opinion.

The Delphi procedure is an accepted methodology for the selection of KIs and QIs in health care. This systematic approach is recommended in research areas hampered by limited evidence to guide clinical practice and disagreement between experts on its interpretation. This method combines evidence-based practice with expert opinion by using a multidisciplinary panel. A large group of experts across diverse locations and areas of expertise can be included anonymously, thus avoiding domination of the consensus process by one or a few experts. This group facilitation technique is designed to transform individual

opinions of experts into group consensus. It includes a series of questionnaires or rounds to gather information and achieve consensus [17, 19, 25].

In this Delphi study, outcomes such as patient and graft survival, graft function, or acute rejection are not included [29]. These are valuable variables but are likely dependent on a number of factors that are not related to the donation procedure (e.g. recipient characteristics, organ procurement, and preservation), and thereby provide less information to guide quality improvements at a donor hospital. Beside QIs related to organ donation, a set of transplant QIs can also be identified. Accountability of the transplant centers on these transplant QIs, will not only stimulate the donor hospitals towards more active engagements in the field but also increase more transparency to the general public [50].

This study was restricted to the phase of KIs and QIs selection. In a next step, further research should explore which KIs (I) are effectively implemented in practice (adherence), and (II) could be improved. These interventions can then be used as a standard to evaluate the quality of existing DBD care and in quality improvement programs. Research should also determine the effect of these interventions on a set of QIs in order to substantiate progress. To this purpose, the three dimensions of structure, process and outcome indicators can be used to assess quality of care [25]. QIs rated as most important were (I) detection of all potential DBDs in the ICU and (II) documentation of cause of not proceeding to donation in potential donors. Reliability and feasibility in practice of this indicator set needs to be tested in both low- and high-volume donor hospitals. With these indicators, donor coordinators could evaluate the quality of the organ donation process at the hospital level.

Our study has several strengths. We used the systematic RAND modified Delphi method, a common and validated technique in which scientific evidence is combined with expert opinion. Our procedure is consistent with the guideline of Boulkedid et al. for using and reporting this consensus technique, in which the median number of panel members was 17 [17]. Our panel was multidisciplinary, with 18 experts covering 5 different functions: intensive care medicine, anesthesiology, intensive care nursing, donor coordination, and transplant

coordination. All involved stakeholders were presented. All the experts completed the three Delphi rounds, which implies that we had a low non-response bias, increasing the validity of the results. These are highly relevant and applicable for clinical teams managing potential DBDs in different health systems, while taking into account each country's legislation and regulations regarding organ donation and transplantation. For being universally accepted, these KIs and QIs need to be tested in an international setting.

However, this study has also some limitations. It is uncertain whether the experts who participated are a true representation of the potentially available experts with preferably a minimum of 10 years' experience and a minimum of 3 organ donors in 2015. On average, only 32% (n = 31) of the Belgian acute care hospitals (n = 98) had more than 3 donors in 2012/2013, therefore the majority of the informed donor coordinators did not meet the criteria to participate in this study [50]. A second limitation of this study is the national setting in which these KIs and QIs were selected. However, international literature was reviewed and the QIs development of the ODEQUS project was performed by a multidisciplinary panel, in which several members have international experience and expertise on the topic. Another potential limitation is the attendance of the physical meeting by only 9 experts because of logistic reasons. However, in this meeting only the KIs and QIs without consensus after round 3 were re-rated by the experts present and the results of this meeting were not included in the final results of the Delphi survey. Finally, only literature published in English, Dutch or French was included in this study, which may include language bias for example to Spanish or German literature.

Conclusions

Using a RAND modified Delphi approach, consensus was reached for a set of 65 KIs for the management of potential DBDs. To assess quality of care for potential DBDs and the impact of this care pathway, 11 QIs were validated for the attributes relevance and feasibility. These KIs are to be considered as a first

description of a standard bundle of care for potential DBDs, while the QIs identified can be incorporated into specific quality improvement programs.

Additional tables: Additional results of the third Delphi round and the physical meeting.

Table 4: Results of the 15 key interventions for which no consensus was reached by the overall panel (n = 18) after the third Delphi round

	Based on literature (L) or expert panel (E)	Median	Tertile 7-9 (%)	Tertile 7-9 (n)	Rating of contribution (%)*
Donor management: general care					
Continue enteral feeding until otherwise instructed by the transplant center.	L	7	56%	10	73%
Continue an appropriate prescription of deep venous thrombosis prophylaxis (low molecular weight heparin).	L	8	72%	13	81%
Ensuring a prescription of low-dose dopamine with a dose of (and not exceeding) 4 µg/kg/min until the aortic clamping and halve the dosage or terminate the infusion earlier when circulatory adverse effects occurred in association with the dopamine infusion, such as tachycardia (> 120 beats per min) or a marked increase in blood pressure (MAP > 110 mm Hg).	L	5	39%	7	59%
Donor management: monitoring					
Measure additional parameters with extended monitoring in case of a patient with hemodynamic instability, by using for instance a pulmonary artery catheter, PiCCO or oesophageal Doppler.	L	6	39%	7	72%
Measure additional parameters with extended monitoring in case of a patient with hemodynamic instability, by using transthoracic or transoesophageal echocardiography. Target ejection fraction: ≥ 50 %.	L	7	67%	12	78%
Periodically re-assess cuff pressure to check if there is no cuff leak and if cuff pressure is between 20-30 cm H_2O to avoid aspiration.	L	8	67%	12	83%

Monitoring of glycemic status. Target blood glucose: ≤ 180 mg/dL.	L	8	72%	13	80%
Ensuring coagulation screening or thromboelastography to target therapy if there is a clinically relevant bleeding.	L	8	67%	12	81%
Donor management: cardiovascular management (hypertension)					
Treat the systemic arterial hypertension related to "adrenergic storm" of severe degree (MAP > 120 mm Hg) and prolonged (> 30 to 60 minutes) with calcium entry blockers or short-acting cardioselective beta-blockers.	L	7	67%	12	77%
Donor management: cardiovascular management (hypotension)					
Avoid hydroxyethyl starch (HES) for intravascular volume replacement.	L	8	72%	13	85%
Donor management: respiratory management					
Perform intermittent nasopharyngeal suction.	L	8	67%	12	85%
Perform intermittent tracheal suction, by preference using a closed circuit.	L	8	67%	12	81%
Donor management: hormone substitution					
Ensuring a prescription of hydrocortisone to reduce the cumulative dose and administration duration of vasopressors: hydrocortisone 50 mg + continuous infusion of 10 mg/h until the aortic clamping.	L	5	17%	3	60%
Ensuring a prescription of methylprednisolone for a potential liver donor: 250 mg bolus + 100 mg/hour until recovery of organs.	L	5	33%	6	61%
Consider thyroid replacement therapy for hemodynamically unstable donors or for potential heart donors with abnormal (<45%) left ventricular ejection fraction.	E	6	39%	7	66%

*rating of contribution = ratio of "sum of ratings on the intervention given by participants" to "sum of ratings on the intervention if all respondents rated the interventions as 'strongly agree'".

Table 5: Results of the quality indicator for which no consensus was reached by the overall panel (n = 18) after the third Delphi round

	Attribute	Median	Tertile 7-9 (%)	Tertile 7-9 (n)
Structure indicator				
Donation team full-time availability.	Relevance	8	72%	13
Formula: availability of the donation team 24/7?	Feasibility	7	61%	11

Table 6: Results of the 4 key interventions for which consensus was reached by 9 experts after the physical meeting

	Based on literature (L) or expert panel (E)	Median	Tertile 7-9 (%)	Tertile 7-9 (n)	Rating of contribution (%)*
Donor management: general care					
Continue an appropriate prescription of deep venous thrombosis prophylaxis (low molecular weight heparin).	L	8	78%	7	85%
Donor management: monitoring					
Periodically re-assess cuff pressure to check if there is no cuff leak and if cuff pressure is between 20-30 cm H_2O to avoid aspiration.	L	9	78%	7	84%
Monitoring of glycemic status. Target blood glucose: ≤ 180 mg/dL.	L	7	78%	7	84%
Ensuring coagulation screening or thromboelastography to target therapy if there is a clinically relevant bleeding.	L	8	78%	7	84%

*rating of contribution = ratio of "sum of ratings on the intervention given by participants" to "sum of ratings on the intervention if all respondents rated the interventions as 'strongly agree'".

Table 7: Results of the 11 key interventions for which no consensus was reached by 9 experts after the physical meeting

	Based on literature (L) or expert panel (E)	Median	Tertile 7-9 (%)	Tertile 7-9 (n)	Rating of contribution (%)*
Donor management: general care					
Continue enteral feeding until otherwise instructed by the transplant center.	L	5	33%	3	63%
Ensuring a prescription of low-dose dopamine with a dose of (and not exceeding) 4 µg/kg/min until the aortic clamping and halve the dosage or terminate the infusion earlier when circulatory adverse effects occurred in association with the dopamine infusion, such as tachycardia (> 120 beats per min) or a marked increase in blood pressure (MAP > 110 mm Hg).	L	5	22%	2	52%
Donor management: monitoring					
Measure additional parameters with extended monitoring in case of a patient with hemodynamic instability, by using for instance a pulmonary artery catheter, PiCCO or oesophageal Doppler.	L	5	0%	0	53%
Measure additional parameters with extended monitoring in case of a patient with hemodynamic instability, by using transthoracic or transoesophageal echocardiography. Target ejection fraction: ≥ 50 %.	L	7	67%	6	77%
Donor management: cardiovascular management (hypertension)					
Treat the systemic arterial hypertension related to "adrenergic storm" of severe degree (MAP > 120 mm Hg) and prolonged (> 30 to 60 minutes) with calcium entry blockers or short-acting cardioselective beta-blockers.	L	3	33%	3	53%
Donor management: cardiovascular management (hypotension)					
Avoid hydroxyethyl starch (HES) for intravascular volume replacement.	L	9	56%	5	60%

Donor management: respiratory management					
Perform intermittent nasopharyngeal suction.	L	9	56%	5	73%
Perform intermittent tracheal suction, by preference using a closed circuit.	L	7	56%	5	67%
Donor management: hormone substitution					
Ensuring a prescription of hydrocortisone to reduce the cumulative dose and administration duration of vasopressors: hydrocortisone 50 mg + continuous infusion of 10 mg/h until the aortic clamping.	L	5	0%	0	40%
Ensuring a prescription of methylprednisolone for a potential liver donor: 250 mg bolus + 100 mg/hour until recovery of organs.	L	3	22%	2	43%
Consider thyroid replacement therapy for hemodynamically unstable donors or for potential heart donors with abnormal (<45%) left ventricular ejection fraction.	E	2	22%	2	42%

*rating of contribution = ratio of "sum of ratings on the intervention given by participants" to "sum of ratings on the intervention if all respondents rated the interventions as 'strongly agree'".

Table 8: Results of the quality indicator for which no consensus was reached by 9 experts after the physical meeting

	Attribute	Median	Tertile 7-9 (%)	Tertile 7-9 (n)
Structure indicator				
Donation team full-time availability.	Relevance	8	78%	7
Formula: availability of the donation team 24/7?	Feasibility	5	33%	3

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Chapter 5

Adherence to guidelines for the management of organ donors after brain death

Pieter Hoste
Patrick Ferdinande
Dirk Vogelaers
Kris Vanhaecht
Eric Hoste
Xavier Rogiers
Kristof Eeckloo
Koenraad Vandewoude

Published in Journal of Critical Care 2019; 49:56-63

5. Adherence to guidelines for the management of organ donors after brain death

Abstract

Purpose: Guideline adherence for the management of a donor after brain death (DBD) is largely unknown. This study aimed to perform an importance-performance analysis of prioritized key interventions (KIs) by linking guideline adherence rates to expert consensus ratings for the management of a DBD.

Materials and methods: This observational, cross-sectional multicenter study was performed in 21 Belgian ICUs. A retrospective review of patient records of adult utilized DBDs between 2013 and 2016 used 67 KIs to describe adherence to guidelines.

Results: A total of 296 patients were included. Thirty-five of 67 KIs had a high level of adherence congruent to a high expert panel rating of importance. Nineteen of 67 KIs had a low level of adherence in spite of a high level of importance according to expert consensus. However, inadequate documentation proved an important issue, hampering true guideline adherence assessment. Adherence ranged between 3 and 100% for single KI items and on average, patients received 72% of the integrated expert panel recommended care set.

Conclusions: Guideline adherence to an expert panel predefined care set in DBD donor management proved moderate leaving substantial room for improvement. An importance-performance analysis can be used to improve implementation and documentation of guidelines.

Introduction

For the management of a potential donor after brain death (DBD), consensus-based guidelines, such as the recommendations of the Society of Critical Care Medicine, provide evidence-based advice aiming at improving quality of care [1]. Guidelines however are not necessarily implemented in practice [2, 3]. A recent systematic review on sustainability of adherence to guidelines by medical professionals identified a limited number of studies and lack of methodological quality, hampering conclusions [4].

Compliance to guidelines for potential DBD is largely unknown and most studies have focused on brain death diagnosis. Adherence to the American Academy of Neurology (AAN) guidelines for determination of brain death, updated in 2010, proved variable [5, 6]. A study in 91 countries revealed differences in perceptions and practices of brain death diagnosis worldwide. In comparison to AAN criteria, significant between-hospital variability was documented in examinations, apnea testing, necessity and type of ancillary testing, time to brain death declaration, as well as the number and minimal qualifications of physicians required for declaration [7].

Besides brain death determination, management of a potential DBD should focus through adherence to guidelines, on different other issues, including maintenance of adequate perfusion to all organ systems, early referral to the organ procurement organizations, and family support [8]. To improve potential DBD management, key interventions (KIs) should be prioritized in order to guarantee high quality care, and impact significantly on patient, donor family, recipient or graft outcomes. However, targeting the right areas for improvement remains difficult. Focusing on all the KIs as a whole can prove burdensome and complex. An importance-performance analysis, originally a marketing research technique, can be an alternative method of prioritizing KIs by linking KI expert panel ratings of importance to the performance indicator of guideline adherence rates [9].

Hence, the aim of this study is to perform such an importance-performance analysis of predefined KIs for the management of a potential DBD by linking guideline adherence rates to expert panel ratings of importance.

Material and methods

Variables

Selection of KIs was based on existing guidelines [10-19], review articles [1, 20-26] and process flow diagrams [27-35]. This selection of KIs was evaluated in a RAND modified three-round Delphi study, aiming at expert consensus on the importance of a KI for the management of a potential DBD. Eighteen experts within Belgium rated all the selected KIs on a 9-point Likert rating scale (score 1 indicating "strongly disagree"; score 9 "strongly agree") on the extent of contribution to quality of care. A KI was considered important with a median score of 7 or more with 75% or more of the ratings within the highest tertile (Likert score: 7-9). Out of a total of 80 KIs assessed throughout the Delphi process, 54 KIs with consensus and 14 KIs without consensus on importance after the third Delphi round were included in the importance-performance analysis. Two KIs without consensus were combined, achieving a final tally of 67 KIs. The KIs were classified into 4 core processes: (I) detection inside the ICU and notification to a transplant center (10 KIs); (II) donor evaluation and characterization (15 KIs); (III) donor management, bundled as: general care (7 KIs), monitoring (14 KIs), cardiovascular management (5 KIs), respiratory management (4 KIs), renal and electrolyte management (6 KIs), hormone substitution (4 KIs); and (IV) post procurement (3 KIs). Twelve KIs were excluded because of impossibility of objective measurement in patient records or restriction of implementation to clinical indication [36].

Study population

This observational, cross-sectional multicenter study was part of the Care Pathway for Donation after Brain Death (CP4DBD) quality improvement research

project, set up by the Belgian federal government to evaluate and improve the care process and quality of care for potential DBDs (or for the donor family, recipient or graft). All 84 Belgian acute hospitals with a recognized donor coordination function were invited in June 2016 to participate through an information letter from the Director General, Department of Healthcare, Federal Public Service Health, Food Chain Safety and Environment. A local study coordinator was appointed in each participating hospital.

Patient inclusion criteria for the study consisted of (1) utilized DBD (actual donor from whom at least one organ was transplanted), (2) adults (≥ 18 years of age), and (3) admitted to an intensive care unit (ICU) between January 1, 2013 and December 31, 2016.

Hospital and ICU characteristics were collected at the start of the study. Patient characteristics, admission data and adherence to guidelines were recorded by retrospective review of in-hospital patient records, using a standardized data extraction form. Registration of the variable (KIs) within the patient record was assessed as “performed”, “not performed” or “not measurable” (and in some cases with not applicable or not possible). Variables were reported as not performed when the patient record explicitly stated the absence of the intervention. KIs were reported as not measurable whenever information on (non-)execution of the KI was missing or ambiguous. This allowed discrimination between non-executed and non-documented variables.

Importance-performance matrix

The relationship between importance and adherence is represented by an importance-performance matrix, as used in similar research [37, 38]. The KI importance dimension was defined by the expert-rating described above [36]. The performance dimension was defined by the adherence rate, measured per KI as the number of patients that received the KI (numerator) / the number of patients for whom the KI was indicated (denominator). A cut-off of 75% was defined to represent a high level of performance. Combining the importance and

performance dimensions forms a matrix consisting of 4 quadrants [9]. The upper 2 quadrants represent important KIs, with high adherence (upper right) and low adherence rate (upper left). The lower 2 quadrants represent the less important KIs, with high adherence (lower right) and low adherence rate (lower left).

Statistical analysis

Continuous data are reported as mean and standard deviation (SD) or median and interquartile range (IQR), dichotomous data presented as absolute numbers and percentage. Analyses at hospital and patient level were performed in SPSS version 24.0.

Ethical approval

The study received ethical approval from the Ethical Committee of the Ghent University Hospital, Belgium (2016/1089, B670201629590) and from the Ethical Committee of each participating hospital.

Results

Hospital and patient characteristics

Twenty-one Belgian hospitals participated in the study, including 4 (19%) university and 17 (81%) non-university hospitals. Their number of hospital beds ranged between 235 and 1995. The number of adult ICU beds which were 24/7 functional for mechanical ventilation ranged between 6 and 94. The average number of patients per hospital included was 14.1 and ranged between 1 and 41.

Over the 4-year study period from January 1, 2013 to December 31, 2016, data from 296 DBDs (mean age 52.4 ± 16.2 years, 155 (53%) male) were retrospectively collected. This sample represented 34% of all DBDs (n = 881) in Belgium in the same time period [39]. The mean organs transplanted per donor (OTPD) was 3.7 ± 1.7 and 150 (51%) had ≥ 4 OTPD. Of the 296 ICU admissions,

195 (66%) were transferred directly from the emergency room of the same hospital and 44 (15%) directly from another hospital. Hospital and patient characteristics are summarized in **Table 1**.

Table 1: Hospital and patient characteristics

Hospital characteristics (*n* = 21)	
	Total
Hospital beds, median (IQR)	542 (451 - 970)
Adult ICU beds, median (IQR)	22 (13 - 44)
Type of hospital, n/N (%)	
University	4/21 (19%)
Non-university	17/21 (81%)
Neurosurgical facilities on site, n/N (%)	21/21 (100%)
Interventional neuroradiology facilities on site, n/N (%)	12/21 (57%)
Transplantation facilities on site, n/N (%)	5/21 (24%)
Number of included patients per hospital, n/N (%)	
< 5	6/21 (29%)
5-10	4/21 (19%)
11-20	6/21 (29%)
21-30	1/21 (5%)
31-40	3/21 (14%)
41-50	1/21 (5%)
Patient characteristics (*n* = 296)	
	Total
Age (in years), mean ± SD	52.4 ± 16.2
Sex, n/N (%)	
Male	155/295 (53%)
Female	140/295 (47%)
Unknown	1
Admission source, n/N (%)	
Emergency room	195/295 (66%)
Other acute care hospital	44/295 (15%)
Operating room	35/295 (12%)
General ward	19/295 (6%)
Other	2/295 (1%)

Unknown	1
Type of admission, n/N (%)	
Medical	145/296 (49%)
Surgical: emergency	90/296 (30%)
Trauma	51/296 (17%)
Surgical: elective	9/296 (3%)
Burns	1/296 (0.3%)
Cause of death	
Anoxia / strangulation	6/296 (2%)
Cardiovascular	19/296 (6%)
Cerebral Ischemia	16/296 (5%)
Intracranial bleeding	156/296 (53%)
Suicide	7/296 (2%)
Trauma (other)	51/296 (17%)
Trauma (road accident)	18/296 (6%)
Tumor	5/296 (2%)
Other	18/296 (6%)
Organs transplanted per donor, mean ± SD (n/N)	3.7 ± 1.7 (1106/296)
% used organs of utilized donors after brain death, n/N (%)	
Kidney right	235/296 (79%)
Kidney left	234/296 (79%)
Liver	242/296 (82%)
Heart	102/296 (34%)
Lung right	132/296 (45%)
Lung left	133/296 (45%)
Pancreas	25/296 (8%)
Intestine	3/296 (1%)

SD = Standard deviation; IQR = Interquartile range.

Importance-performance analysis

The importance-performance matrix is presented in **Figure 1**. Thirty-five of the 54 high level of importance KIs had a level of performance above 75% (upper right quadrant). Nineteen of the 54 high level of importance KIs were performed for ≤ 75% of the patients (upper left quadrant) and can thus be classified as high

priority interventions to improve the management of a potential DBD. Eleven of these underused KIs do not achieve a threshold performance of 50%. In the lower left quadrant, 10 low priority KIs are shown with both low importance and performance. Three overused KIs were identified (lower right quadrant) with low importance and nevertheless high performance.

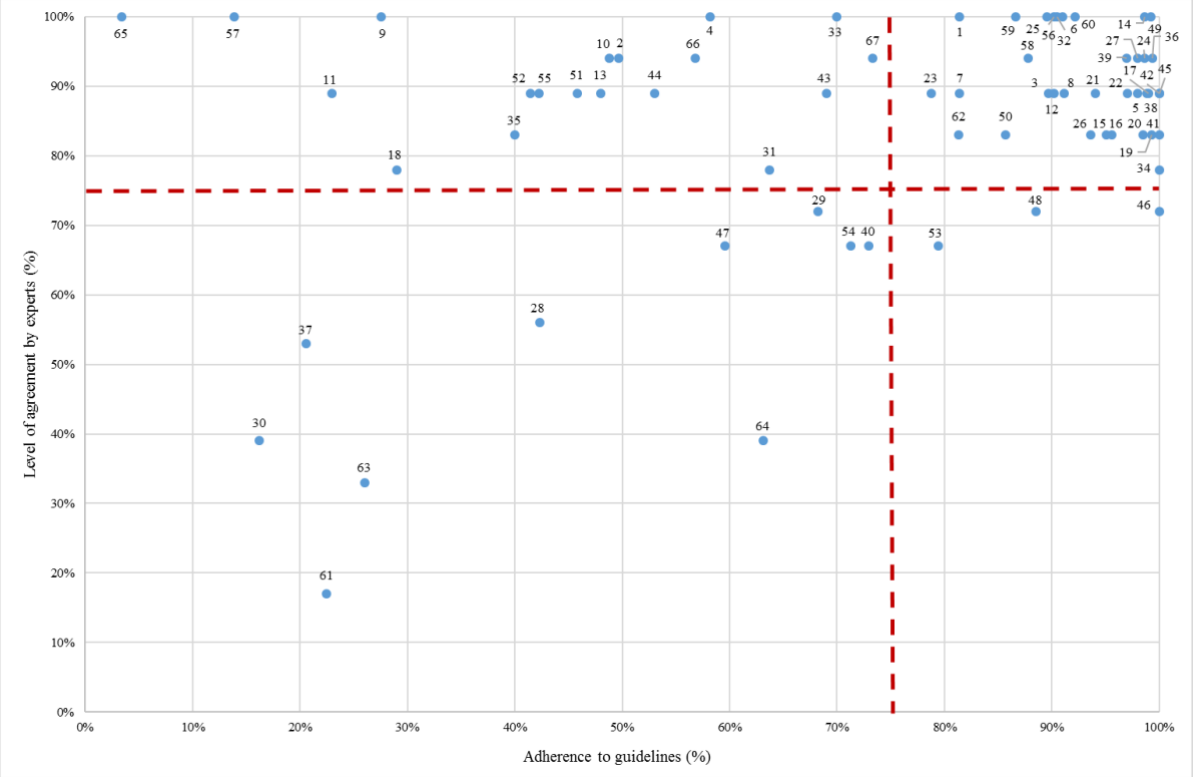

Figure 1: Importance-performance analysis. The numbers in Figure 1 correspond with the key interventions mentioned in Table 2. The horizontal line shows the high or low level of importance (75%), whilst the vertical line shows the high or low level of performance (75%). Upper right quadrant: good performance of high priority key interventions; upper left quadrant: bad performance of high priority key interventions; lower left quadrant: good performance of low priority key interventions; lower right quadrant: bad performance of low priority key interventions

Adherence to guidelines

Table 2 summarizes adherence and expert consensus rates for all KIs. Adherence to individual KIs varied between 100% (blood gas analysis on a regular basis) and 3% (written reporting of detection of serious adverse events). Furthermore, low adherence to high importance guidelines (upper left quadrant

in the importance-performance matrix) (< 50% and N > 100) was found for the following interventions: reviewing, if polyuria, of the medical history, urinary and blood sample to exclude secondary polyuria (14%); interviewing family and/or other relevant sources to obtain the medical and behavioral history (23%); information to the family about brain death diagnosis (28%); installation of lung protective ventilation (41%); oral hygiene every 6 h (42%); written report of the clinical examination of the potential donor (48%); and information to the family about the possibility of organ and tissue donation and the outcome of the National Register consultation (49%). None of the patients received the full care set of 54 KIs. On average, patients received 72% of recommended care. For the donor management care activities, the received recommended care was 86% for general care (4 KIs), 84% for monitoring (11 KIs), 77% for cardiovascular management (3 KIs), 42% for respiratory management (2 KIs), 74% for renal and electrolyte management (5 KIs) and 81% for hormone substitution (1 KI).

Table 2: Adherence to the key interventions for the management of a potential donor after brain death

Number	Intervention	Performance rate n/N (%)	Not documented n/N (%)	Expert consensus rate (%) [36]
	Detection inside the ICU and notification to a transplant center			
1	Detection of the potential donor after brain death based on defined clinical triggers.	241/296 (81%)	52/296 (18%)	100%
2	Notification to the local donor coordinator at the time these criteria are met.	147/296 (50%)	148/296 (50%)	94%
3	Assessment of the prerequisites prior to the clinical evaluation of brain death.	1871/2087 (90%) [a]	20/2087 (1%) [a]	89%
	a) Coma, irreversible, and cause known.	261/261 (100%)	0/261 (0%)	
	b) Neuroimaging compatible with coma.	258/261 (99%)	0/261 (0%)	
	c) Central nervous system depressant drug effect absent (if indicated, toxicology screen; if barbiturates given, serum level <	249/261 (95%)	4/261 (2%)	

	10 µg/mL).			
	d) No evidence of residual paralytics or neuromuscular blocking agents (electrical stimulation if paralytics used).	257/261 (98%)	3/261 (1%)	
	e) Absence of severe acid-base, electrolyte, and endocrine abnormality.	217/261 (83%)	1/261 (0.4%)	
	f) Normothermia or mild hypothermia (core temperature > 36 °C).	155/261 (59%)	1/261 (0.4%)	
	g) Systolic blood pressure > 100 mmHg. Vasopressors may be required.	224/261 (86%)	1/261 (0.4%)	
	h) No spontaneous respiration.	250/260 (96%)	10/260 (4%)	
4	Family approach (bad news conversation and support).	341/586 (58%) [b]	243/586 (41%) [b]	100%
	a) Delivering bad news about the hopeless, medical situation.	198/293 (68%)	95/293 (32%)	
	b) Support of the family (physician, nurse, social assistant, psychologist, pastoral service…).	143/293 (49%)	148/293 (51%)	
5	Notification of the potential donor after brain death by an ICU physician to a transplant center.	290/296 (98%)	6/296 (2%)	89%
6	Determination of brain death	808/888 (91%) [c]	75/888 (8%) [c]	100%
	a) According to the latest medical knowledge concerning the subject.	260/296 (88%)	32/296 (11%)	
	b) By three physicians.	274/296 (93%)	21/296 (7%)	
	c) Excluding those who are treating the receptor or will perform the procurement or transplantation.	274/296 (93%)	22/296 (7%)	
7	Legal declaration of death.	241/296 (81%)	31/296 (10%)	89%
8	Notification to the legal authorities if the cause of death was unknown or suspicious.	72/79 (91%)	7/79 (9%)	89%

9	Information to the family about the diagnosis of brain death.	81/294 (28%)	213/294 (72%)	100%
10	Information to the family about the possibility of organ and tissue donation and the outcome of the National Register.	286/586 (49%) [d]	298/586 (51%) [d]	94%
	a) Information to the family about the possibility of organ and tissue donation.	271/294 (92%)	23/294 (8%)	
	b) Information to the family about the outcome of the National Register.	15/292 (5%)	275/292 (94%)	
	c) Preferably in a separated conversation after family understand the diagnosis of brain death.	34/294 (12%)	258/294 (88%)	
	d) Preferably in a separated conversation after family accept the diagnosis of brain death.	33/294 (11%)	259/294 (88%)	
	Donor evaluation and characterization			
11	Interviewing family and/or other relevant sources to obtain the medical and behavioral history.	68/296 (23%)	223/296 (75%)	89%
12	Reviewing medical charts to obtain the medical and behavioral history.	267/296 (90%)	27/296 (9%)	89%
13	Clinical examination of the potential donor: written report.	142/296 (48%)	23/296 (8%)	89%
14	Blood sample.	292/296 (99%)	4/296 (1%)	100%
15	ABO and rhesus blood group or additional laboratory tests.	563/592 (95%) [e]	3/592 (1%) [e]	83%
	a) ABO and rhesus blood group.	273/296 (92%)	3/296 (1%)	
	b) Additional laboratory tests.	290/296 (98%)	0/296 (0%)	
16	Urine sample: measurement of sediment, protein & glucose.	283/296 (96%)	4/296 (1%)	83%
17	Chest X-ray: mandatory for each potential donor and to allow evaluation of a potential lung and/or heart donor.	293/296 (99%)	0/296 (0%)	89%
18	Bronchoscopy (on request of the	114/393	23/393	78%

	transplant center, all the following interventions are not always necessary)	(29%) [f]	(6%) [f]	
	a) To allow evaluation of a potential lung donor.	57/135 (42%)	7/135 (5%)	
	b) To collect samples for microbiological tests.	39/127 (31%)	6/127 (5%)	
	c) To perform a bilateral bronchoalveolar lavage (BAL) to clear mucous plugs or blood clots that may contribute to impaired oxygenation.	18/131 (14%)	10/131 (8%)	
19	Arterial blood gas: to allow evaluation of a potential (lung) donor.	134/135 (99%)	1/135 (1%)	83%
20	Arterial blood gas after 10 min ventilation with FiO_2 100% & 5 cm H_2O PEEP: to allow evaluation of a potential lung donor.	133/135 (99%)	0/135 (0%)	83%
21	12 lead ECG: to allow (partial/initial) evaluation of a potential heart donor.	95/101 (94%)	1/101 (1%)	89%
22	Cardiac ultrasound: to allow evaluation of a potential heart donor.	99/102 (97%)	0/102 (0%)	89%
23	Coronary angiography: if cardiac ultrasound is acceptable but other comorbidities are present.	26/33 (79%)	1/33 (3%)	89%
24	Abdominal ultrasound (or CT scan): to allow evaluation of a potential liver, pancreas and/or kidney donor.	287/291 (99%)	1/291 (0%)	94%
25	Collection of the minimum data on a donor information form as requested by the transplant center for the characterization of organs and donor.	265/296 (90%)	26/296 (9%)	100%
	Donor management: general care			
26	Presence of an arterial and central venous line.	277/296 (94%)	1/296 (0.3%)	83%
27	Continuation of appropriate antibiotic therapy and other life supporting pharmacotherapy.	290/296 (98%)	0/296 (0%)	94%
28	Continuation of enteral feeding (until otherwise instructed by the transplant center).	11/26 (42%)	0/26 (0%)	56%
29	Continuation of deep venous thrombosis prophylaxis if there were no	73/107	1/107	72%

	contraindications.	(68%)	(1%)	
30	Prescription of low-dose dopamine with a dose of (and not exceeding) 4 µg/kg/min until the aortic clamping.	48/296 (16%)	1/296 (0.3%)	39%
	Halving the dosage or ending the infusion when circulatory adverse effects occurred in association with the dopamine infusion, such as tachycardia or a marked increase in blood pressure.	15/32 (47%)	0/32 (0%)	
31	Prevention of hypothermia.	93/146 (64%)	28/146 (19%)	78%
32	Reduction of the vasopressor dose to the minimal level to maintain hemodynamic stability.	238/263 (90%)	1/263 (0.4%)	100%
	Donor management: monitoring			
33	Monitoring of the core body temperature.	207/296 (70%)	58/296 (20%)	100%
34	ECG monitoring of heart rate.	296/296 (100%)	0/296 (0%)	78%
35	New 12-lead ECG for a potential heart donor if there are subsequent changes in monitored complexes.	6/15 (40%)	1/15 (7%)	83%
36	Invasive arterial pressure monitoring.	294/296 (99%)	1/296 (0.3%)	94%
37	Measurement of additional parameters with extended monitoring (e.g. PICCO, pulmonary artery catheter…) in case of a patient with hemodynamic instability.	14/68 (21%)	0/68 (0%)	53% [g]
38	Availability of a recent chest X-ray for a potential lung and/or heart donor.	174/176 (99%)	0/176 (0%)	89%
39	Monitoring of ventilator parameters.	287/296 (97%)	6/296 (2%)	94%
40	Assessment of cuff pressure, periodically, to check if there is no cuff leak and cuff pressure is 20-30 cm H_2O to avoid aspiration.	216/296 (73%)	35/296 (12%)	67%
41	Peripheral oxygen saturation monitoring.	296/296 (100%)	0/296 (0%)	83%
42	Blood gas analysis on a regular basis.	296/296 (100%)	0/296 (0%)	89%
43	Bronchial secretion sample for	167/242	25/242	89%

	microscopy and culture if secretions are present.	(69%)	(10%)	
44	Monitoring of urine output (hourly).	157/296 (53%)	1/296 (0%)	89%
45	Measurement of blood electrolytes on a regular basis.	296/296 (100%)	0/296 (0%)	89%
46	Monitoring of glycemic status.	296/296 (100%)	0/296 (0%)	72%
	Donor management: cardiovascular management			
47	Treatment of hypertension related to "adrenergic storm" of severe degree (MAP > 120 mmHg) and prolonged (> 30 to 60 min) with calcium entry blockers or short-acting cardioselective beta-blockers.	53/89 (60%)	0/89 (0%)	67%
48	No prescription of hydroxyethyl starch (HES) for intravascular volume replacement.	247/279 (89%)	1/279 (0.4%)	72%
49	Prescription of vasoactive drugs when correction of the volume deficit fails to achieve the threshold hemodynamic goals.	263/265 (99%)	0/265 (0%)	100%
50	Treatment of bradycardia causing hemodynamic instability with a short acting β-adrenergic agonist (epinephrine / dopamine / dobutamine / isoprenaline) or occasionally transvenous pacing.	6/7 (86%)	0/7 (0%)	83%
51	Treatment of tachycardia.	38/83 (46%)	0/83 (0%)	89%
	Donor management: respiratory management			
52	Installation of a lung protective ventilation.	491/1184 (41%) [h]	148/1184 (13%) [h]	89%
	a) Minimum FiO_2 to obtain a PaO_2 between 80 and 100 mmHg.	107/296 (36%)	1/296 (0.3%)	
	b) Tidal volume (Vt): 6-8 mL/kg (ideal body weight).	134/296 (45%)	45/296 (15%)	
	c) Plateau pressure: < 30 cm H_2O.	199/296 (67%)	93/296 (31%)	
	d) PEEP (Positive End Expiratory Pressure): 8-10 cm H_2O.	51/296 (17%)	9/296 (3%)	

53	Intermittent nasopharyngeal suction.	235/296 (79%)	42/296 (14%)	67%
54	Intermittent tracheal suction.	211/296 (71%)	44/296 (15%)	67%
55	Oral hygiene every 6 h.	125/296 (42%)	29/296 (10%)	89%
	Donor management: renal and electrolyte management			
56	If oliguria, no prescription of diuretic after treating of hypovolemia, hypotension and cardiac dysfunction.	83/92 (90%)	1/295 (0.3%)	100%
57	If diabetes insipidus, reviewing of the medical history, urinary and blood sample to exclude secondary polyuria.	18/130 (14%)	111/130 (85%)	100%
58	If diabetes insipidus, adequate diagnose of diabetes insipidus.	115/131 (88%)	1/131 (1%)	94%
59	If diabetes insipidus, treatment of diabetes insipidus with sufficient fluid volume replacement to compensate polyuria and anti-diuretic hormone replacement.	110/127 (87%)	0/127 (0%)	100%
60	Treatment of electrolyte disturbances.	176/191 (92%)	1/191 (1%)	100%
	Donor management: hormone substitution			
61	Prescription of hydrocortisone to reduce the cumulative dose and administration duration of vasopressors.	60/267 (22%)	1/267 (0.4%)	17%
62	Appropriate prescription of insulin if treating hyperglycemia to achieve a target glucose level of 180 mg/dL or less.	187/230 (81%)	0/230 (0%)	83%
63	Prescription of methylprednisolone (250 mg bolus + 100 mg/h until recovery of organs) for a potential liver donor.	63/242 (26%)	0/242 (0%)	33%
64	Thyroid replacement therapy for hemodynamically unstable donors or for potential hearts donors with abnormal (< 45%) left ventricular ejection fraction.	12/19 (63%)	2/19 (11%)	39%

	Post procurement			
65	Written report that detection of serious adverse events was performed.	10/296 (3%)	19/296 (6%)	100%
	If a serious adverse event was detected, registration and reporting to the transplant center.	5/6 (83%)	1/6 (17%)	
66	Debriefing about the results of the transplantation.	663/1167 (57%) [i]	361/1167 (31%) [i]	94%
	a) The relatives	182/283 (64%)	96/283 (34%)	
	b) The health care professionals	178/296 (60%)	96/296 (32%)	
	c) The primary care physician	98/296 (70%)	82/296 (28%)	
67	Exclusion of any medical, pharmaceutical or hospital costs after the determination of brain death and legal declaration of death on the hospitalization invoice.	217/296 (73%)	27/296 (9%)	94%

[a] 3 = 3a + 3b + 3c + 3d + 3e + 3f + 3g + 3h, [b] 4 = 4a + 4b, [c] 6 = 6a + 6b + 6c, [d] 10 = 10a + 10b, [e] 15 = 15a + 15b, [f] 18 = 18a + 18b + 18c, [g] Mean results of 2 key interventions, [h] 52 = 52a + 52b + 52c + 52d, [i] 66 = 66a + 66b + 66c

Discussion

The present study shows the baseline level of guideline adherence to a broad set of 67 KIs in 21 Belgian hospitals and demonstrates significant variability between individual KIs. On average, patients received 72% of the recommended care set. For the 54 KIs that were rated by experts as highly important, 35 KIs were performed for ≥ 75% of the patients. These results have no direct benchmark but seem to score better than adherence to recommended care in general, as reported by McGlynn et al. [3], in which patients received on average 55% of recommended care.

Importance-performance analysis can prove useful to hospitals to select focused, preferably high level of importance/low level of performance, care interventions to improve guideline adherence and documentation of recommended care, as an alternative to the more burdensome indiscriminate approach of implementing the whole set of recommendations. Based on the importance-performance analysis in the present study, 19 such priority KIs could be identified. For some KIs the low performance rate is likely related to under documentation. Apart from the impact of under documentation on determining true guideline adherence, documentation shortages as such may represent a quality problem in daily practice for any complex care process, in terms of coordination and continuity of care. When an intervention is not mentioned in the patient record, other healthcare providers are not aware of its performance, possibly leading to duplication of interventions.

Notification of the local donor coordinator at the time a potential DBD is detected based on defined clinical triggers is a high level of importance KI but had a performance of only 50%. However, due to inadequate documentation in up to 50% of patients, true guideline adherence is unknown. Nowadays, in many European Union member states including Belgium, donor coordinators have been appointed in hospitals with an intensive care unit, where organ retrieval from deceased donors can be considered. Donor coordinators have clearly defined responsibilities in establishing, managing and reviewing the deceased donation processes in their hospital [40]. A recent Spanish audit of the donation pathway of 1970 patients with devastating brain injury, showed that there was less family objection to organ donation when the donor coordinator participated in the interview [41]. Three consensus KIs related to the approach of the donor families, e.g., (a) bad news conversation and support, (b) information about the diagnosis of brain death, and (c) information about the possibility of organ and tissue donation and the outcome of the National Register consultation had a performance of, respectively, 58%, 28% and 49%. However, due to inadequate documentation of these three KIs in the patient records, respectively, 41%, 72%, 51%, true guideline adherence again could not be certified. Further efforts should also focus on implementation strategies in donor hospitals to improve quality of KI documentation. These specific KIs should be priorities as it is well recognized

that the approach and skills of health professionals discussing organ donation are key influences on decisions made by families regarding organ donation [42].

To obtain an accurate, reliable and objective medical and behavioral history, health care professionals should perform an interview with the relatives and/or other relevant sources. In our study, the performance rate of this consensus KI was only 23%. This interview is however crucial to donor evaluation to minimize any risks associated with the transmission of diseases, together with a detailed review of the medical records, assessment of the medical and behavioral history, full clinical examination, findings of post-mortem autopsy, if performed, and laboratory tests [40]. However, due to inadequate documentation in up to 75% of patients, true guideline adherence is unknown. Another priority in donor evaluation should be the performance of the documentation of a clinical examination of the potential donor, as only 48% of the patients received this consensus KI. In our study, the performance rate of a bronchoscopy in the assessment of lung explantation was 42%, to collect samples for microbiological tests 31%, and to perform a bilateral bronchoalveolar lavage to clear mucous plugs or blood clots that may contribute to impaired oxygenation 14%. Transplant centers should primarily focus on these KIs, related to bronchoscopy, because these KIs are only performed on their request prior to referral.

Traditionally, normothermic body temperature, which may require active warming, is aimed for in DBDs. In our study two KIs, monitoring of central ("core") body temperature and using of warming mattress, blankets or warmed intravenous if hypothermia (temperature < 35 °C) had a performance of 70% and 64%, respectively. However, mild hypothermia (34 to 35 ˚C) after declaration of death according to neurologic criteria may lead to better allograft outcomes. In a comparison of two targeted temperature ranges (34 to 35 ˚C and 36.5 to 37.5 ˚C), hypothermia reduced the frequency of delayed graft function in kidney transplantation, defined as a requirement for dialysis during the first week after transplantation [43]. Further research is needed to determine the utility of hypothermia in this setting. Other monitoring priorities include a new 12-lead ECG for a potential heart donor in response to changes in monitored complexes (performance rate: 40%), bronchial secretion sample for microscopy and culture

if secretions are present (performance rate: 69%), and hourly monitoring of urine output, for early detection of diabetes insipidus (performance rate: 53%).

In the absence of literature specific to DBD, recent guidelines have recommended to follow established advanced cardiopulmonary life support guidelines to manage arrhythmias. In particular, changes in adrenergic responses in the course of brain death predispose the potential DBD to a myriad of transient and sustained arrhythmias requiring medical management [1]. In our study, 28% of the DBDs had a tachycardia, but only 45% of these patients received treatment.

As a priority, respiratory management consists of the implementation of ventilator strategies utilizing low stretch protocols and measures to recruit atelectatic lung to enhance lung recovery [1, 23, 44]. The mean performance rate of a lung protective ventilation strategy in our study was 41%, with a performance rate of 36% for a minimum FiO_2 to obtain a PaO_2 between 80 and 100 mmHg, 45% for a tidal volume between 6 and 8 mL/kg, 67% for a plateau pressure < 30 cm H_2O, and 17% for a positive end expiratory pressure between 8 and 10 cm H_2O. Besides, Hua et al. recently concluded in a systematic review that oral hygiene care reduces the risk of developing ventilator-associated pneumonia from 25% to about 19%. In our study, the performance rate for oral hygiene care every 6 h was 42%, demonstrating once again room for improvement [45].

In our study, 43% of the patients had diabetes insipidus. The performance rate to review the medical history, urinary and blood sample to exclude secondary polyuria (osmotic, induced or adapted) was respectively 14%, undoubtedly an underestimation of true guideline adherence in view of inadequate documentation in up to 85% of cases.

To conclude, three post procurement KIs should be prioritized based on our importance-performance analysis. These interventions are expected to fall under the responsibility of a well-trained donor coordinator on the ICU. The performance rate of a written report on detection of serious adverse events was only 3%, debriefing about the results of the transplantation to the relatives, health care professionals and primary care physician 57%, and ensuring that the

hospitalization invoice of the patient is excluded of any medical, pharmaceutical or hospital costs after the determination of brain death and legal declaration of death 73%.

A first limitation of the study consists of possible selection bias, as only the utilized DBDs are included. Hospitals without utilized but with potential DBDs could not participate in the study. Besides, potential DBDs lost along the organ donation pathway were not included in the dataset, but could also provide useful information. Resource and time constraints excluded a detailed chart review of all deceased ICU patients in participating hospitals. Second, an inclusion criterion on hospital level to participate in the study was the willingness to develop and implement a care pathway for donation after brain death after the study. This may bias selection of participating hospitals towards those with already present intrinsic motivation towards standardizing care and management of potential DBD. A final and major limitation consists of the frequent underestimation of the true guideline adherence as analysis was restricted to information available in the patient records with obvious suboptimal clinical documentation. This however can be considered as a major finding in itself.

To our knowledge, this is the first audit evaluating clinical practice in the entire donation pathway. The main novelty resides in the use of an importance-performance analysis as an approach for prioritizing interventions in improving quality of care for potential DBDs. The participating hospitals in this CP4DBD quality improvement research project received a detailed report with the guidelines upon which these KIs were based, together with feedback on actual organization of the care process. In addition, all participating hospitals received training on care pathway development and implementation. An evidence-based care pathway and this benchmarking approach in donor hospitals can be used as a method to reduce clinical variability and improve both documentation as well as adherence [46-48]. Documentation, monitoring, and evaluation of variances and outcomes are one of the essential components of a care pathway [49]. The introduction of a checklist can be a useful tool to support this and to address the proven documentation need in the donation pathway. Growing evidence in

several areas of healthcare has supported the introduction of such tools in clinical practice [50-52].

In conclusion, guideline adherence to an expert panel predefined care set in DBD donor management proved moderate with substantial room for improvement. These findings underscore the need for a strategy to improve implementation and documentation of evidence-based guidelines, for which an importance-performance analysis may prove useful.

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Chapter 6

Recommendations for further improvement of the deceased organ donation process in Belgium

Pieter Hoste
Patrick Ferdinande
Eric Hoste
Kris Vanhaecht
Xavier Rogiers
Kristof Eeckloo
Dominique Van Deynse
Didier Ledoux
Koenraad Vandewoude
Dirk Vogelaers

Published in Acta Clinica Belgica 2016; 71(5): 303-312.

6. Recommendations for further improvement of the deceased organ donation process in Belgium

Abstract

Belgium has achieved high deceased organ donation rates but according to the medical record data in the Donor Action database, deceased potential donors are still missed along the pathway. Between 2010 and 2014, 12.9 ± 3.3% of the potential donors after brain death (DBD) and 24.6 ± 1.8% of the potential donors after circulatory (DCD) death were not identified. Conversion rates of 41.7 ± 2.1% for DBD and 7.9 ± 0.9% for DCD indicate room for further improvement. We identify and discuss different issues in the monitoring of donation activities, practices and outcomes; donor pool; legislation on deceased organ donation; registration; financial reimbursement; educational and training programs; donor detection and practice clinical guidance. The overall aim of this position paper, elaborated by a Belgian expert panel, is to provide recommendations for further improvement of the deceased organ donation process up to organ procurement in Belgium.

Introduction

Organ transplantation is the preferred therapy for many patients with end-stage diseases since both survival rates and quality of life are superior in allograft recipients as compared to similar patients without transplantation [1, 2]. However, insufficient availability of donor organs to meet the existing demand is a major issue in the field of transplantation [3]. More than 1200 people in Belgium [4], 65,000 in the European Union [5] and 78,000 in the United States [6] are currently on waiting lists for a lifesaving organ transplant. Unfortunately, each year between 80 and 120 patients die while on Belgian waiting lists [4]. Belgium, a country with a proactive donor legislation for the last 30 years, reported an average of 26.7 deceased donors per million inhabitants over the last decade, within the top five highest donor recruitment rates worldwide [4, 7]. The legislative framework together with local, regional and national initiatives by the Belgian Transplantation Society (BTS) and its section of transplant coordinators on the one hand and the national awareness campaign (BELDONOR) on the other hand, positively impacted on donor numbers (Figure 1). Within the BELDONOR campaign, the GIFT project was launched in 2006 to focus on the commitment of health care professionals in intensive care and/or emergency units of acute hospitals. Through this project, the department of Health Care of the Belgian federal government intended to identify the bottlenecks in organ donation in order to optimize donor identification [8]. But in spite of these favorable donor rates, medical record review data showed that deceased potential donors are missed along the donation pathway because of lack of identification or referral, failure to approach relatives or objections to donation. In accordance with the European directive 2010/45/EU, the GIFT project was strengthened in 2012 by the implementation of a local donor coordination function in every hospital with a potential for organ donation, coupled with a cooperation agreement with a transplant center.

Monitoring of donation activities, practices and outcomes

Despite international recommendations on their development, quality assurance programs (QAPs) remain limited to a few countries in Europe [9-11]. QAPs are an important tool to ensure continuous improvement in the performance of the deceased donation process [11]. In Belgium the methodology developed by the Donor Action Foundation was applied as QAP between 2006 and 2015, in order to assess donation performance of individual hospitals. The donor coordinators participating in the GIFT project were asked to yearly register all deaths on their Intensive Care Unit (ICU) in the Donor Action database, using a protected website. This Donor Action program used a systematic approach toward achieving quality in the donation process from deceased donors at hospital level, taking into account the five steps of the donation pathway: donor identification, referral, family approach and consent, donor maintenance and organ retrieval [12].

Although this program had the potential to assess individual hospitals' donation performance, identify bottlenecks and suggest areas for improvement of their donation process [12], it had some disadvantages. There has been no update for many years. When conducting the retrospective medical audit of all deaths in an intensive care unit, a donor coordinator could select, based on the medical and social history, the admission diagnosis, and/or concurrent disease, contraindications for organ and tissue donation. Unfortunately, this list of contraindications was no longer consistent with the internationally accepted criteria. Donor hepatitis C virus seropositivity is for example not an absolute contraindication to organ donation. These organs may be directed for use in hepatitis C virus positive recipients [13-15]. A restriction of this list would be appropriate to reveal the true number of potential donors in Belgium. In order to prevent inadequate selection of potential donors, it is advisable that each potential donor should be discussed with the transplant center. The concerned transplant program will decide on the quality of the organs and tissues to be transplanted and the contraindications for organ and tissue donation, taking into account the evolving criteria. Another limitation of this retrospective audit was

the lack of external audit of completeness and accuracy of the data collected by the donor coordinators.

The federal government implemented 'GIFT Action', a simplified monitoring tool on donor detection aiming at minimizing administrative workload while collecting more complete and relevant information in 2016.

In the past, most donor hospitals collected the data on donor detection in ICUs only. Inclusion of emergency departments, coronary care units and acute neurological admissions such as in stroke units would probably increase the potential donor pool [16, 17].

Furthermore, this QAP could be improved by recording of data in two complementary phases. The first phase consists of an internal evaluation or continuous self-reporting which is already carried out by the hospital donor coordinators, using this anticipated sequel of Donor Action. This remains a retrospective analysis of the medical records of deaths in the intensive care unit and other key hospital departments to identify potential donors. Each case should be analyzed to verify whether the potential donor was referred to the transplant center and, if not, the reasons should be recorded. All reasons for non-conversion of potential donors should be assessed and registered: brain death diagnosis not completed, medical unsuitability, donor management problems, family refusals, refusal in state registry, judicial refusal, lack of appropriate recipients or organizational problems.

Similar to the Spanish QAP, a second phase can consist of a periodical external evaluation of the deceased donation process, with three separate goals: firstly, to verify whether the internal evaluation has been properly performed; secondly, to evaluate the performance through the identification of non-referred potential donors and the analysis of other causes for potential donor loss, and, finally, to make recommendations for improvement to be addressed to donor coordinators but also to hospital managers. De la Rosa et al. observed that a merely self-evaluating approach seems to underestimate the donor potential. External audits in Spain revealed that the number of actual donors could increase

by 21.6% if all potential donors were identified and preventable losses avoided [18]. Similar to Spain, this external evaluation was also included in the methodology of the Organ Donation European Quality System (ODEQUS) project in 2010-2013 [19]. In Belgium, this external audit component can be carried out by expert donor coordinators coming from a different region [20]. The auditor could have for instance a critical care specialist background, with at least 5 years' experience as donor coordinator, work in an audited hospital and have received specific training in the methodology [18].

This auditing model should be based on a set of quality indicators to assess the organizational structures, clinical procedures and outcomes in donor hospitals. This offers the opportunity of using benchmarks and best practices guidance [11, 19]. Both benchmarks and best practices still need to be defined for Belgium. In contrast to the present situation, this critical data should be published in an annual national report to ensure transparency of practices. Inter alia, these data could be more representative for the number and the causes of losses of potential deceased donors in Belgium, than the yearly published national donation and organ transplantation statistics collected by the section of transplant coordinators of the Belgian Transplantation Society. The latter only include the potential donors who are referred to a transplant center [21-23]. In addition to a set of quality indicators to monitor the donation process, indicators should be developed specific to the transplantation process. Accountability of the transplant centers on transplanted organ outcome such as long-term graft and patient survival, delayed graft function, refused and discarded organ rates will not only stimulate the donor hospitals but also increase the transparency for the general public.

Donor pool

Deceased organ donation is possible from donors after brain death (DBD) and donors after circulatory death (DCD). Recently a group of Belgian experts proposed a modification of the Maastricht classification for donors after circulatory death, presented in Table 1. It classifies the DCD on whether the

situation is uncontrolled (categories I and II) or controlled (categories III, IV, and V) [24].

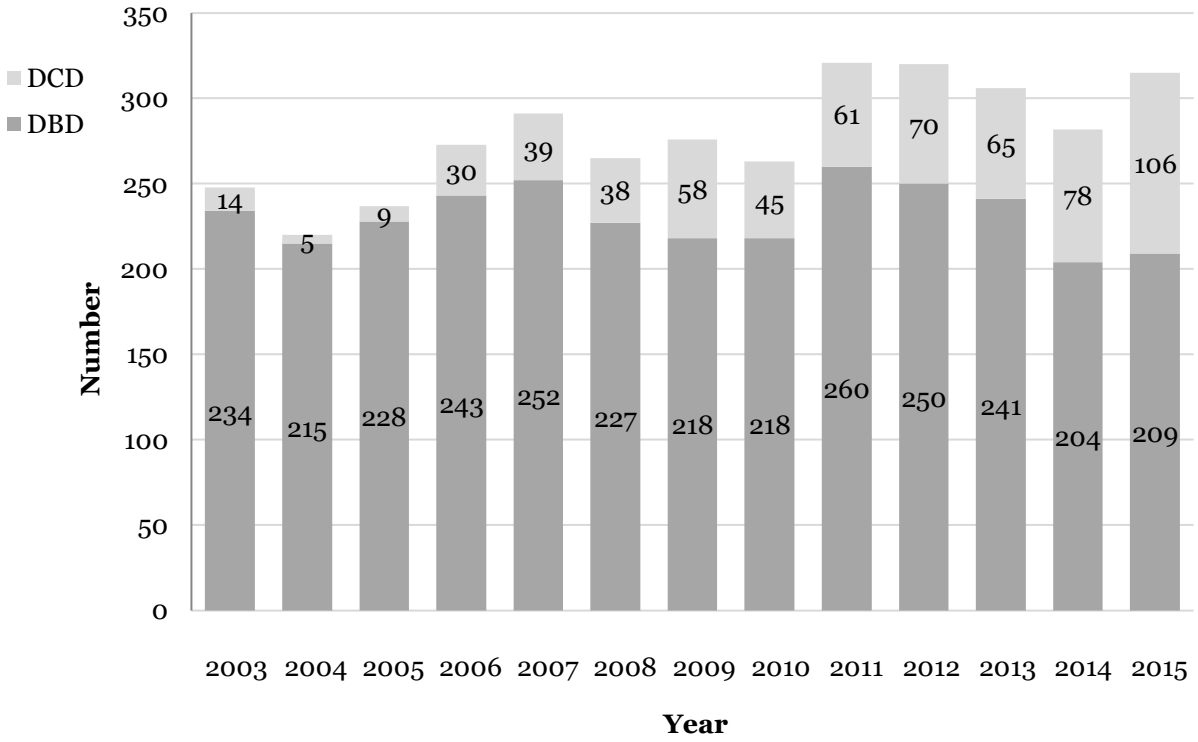
Table 1: Belgian modified classification for donors after circulatory death [24]

Uncontrolled DCD		
I	Death on arrival	Includes victims of a sudden death, whether traumatic or not, occurring out of or in the hospital and who, for obvious reasons, have not been resuscitated.
II	Unsuccessful resuscitation	Includes patients who have a cardiac arrest and in whom cardiopulmonary resuscitation has been applied and was unsuccessful. Cardiac arrest occurs out of or in the hospital, being attended by healthcare personnel with immediate initiation of cardiopulmonary resuscitation.
Controlled DCD		
III	Awaiting cardiac arrest	Includes patients in whom withdrawal of life-sustaining therapies is applied, as agreed on within the healthcare team and with the relatives or representatives of the patient.
IV	Cardiac arrest while brain death	Includes patients who have a cardiac arrest during a DBD procedure.
V	Euthanasia	Includes patients who grant access to medically assisted circulatory death.

Notes: DCD: donation after circulatory death; DBD: donation after brain death

An utilized donor is a donor from whom at least one organ is transplanted [25]. In 2015, out of 315 utilized deceased organ donors respectively 209 (66.3%) were DBD and 106 (33.7%) DCD (Figure 1). Compared to 2011, the DBD donation rate decreased with 19.6% from 260 donors in 2011 to 209 donors in 2015 [4]. It is essential for all donor hospitals and transplant centers to avoid a further decrease of DBD, because this inevitably leads to less transplantable organs. The average number of transplanted organs is higher in DBD compared to DCD (3.3 vs 2.3 organs/donor in 2015, respectively) [21]. Moreover, organs from uncontrolled and controlled DCD may be of inferior quality because they are exposed to an uncontrollable warm ischemia period between switch off of life-sustaining therapies and declaration of death [26-28]. The number of DCD has reached its highest number ever. There were respectively 96 controlled DCD category III (awaiting cardiac arrest), 2 controlled DCD category IV (cardiac

arrest while brain death) and 8 controlled DCD category V (euthanasia) in 2015 [4].



Total DBD	**234**	**215**	**228**	**243**	**252**	**227**	**218**	**218**	**260**	**250**	**241**	**204**	**209**
DCD Cat I	0	0	0	0	0	0	0	0	0	0	0	0	0
DCD Cat II	1	0	3	2	1	1	1	3	3	1	0	0	0
DCD Cat III	11	5	4	26	37	37	55	40	56	64	62	74	96
DCD Cat IV	2	0	1	1	0	0	0	1	1	2	0	0	2
DCD Cat V	0	0	1	1	1	0	2	1	1	3	3	4	8
Total DCD	**14**	**5**	**9**	**30**	**39**	**38**	**58**	**45**	**61**	**70**	**65**	**78**	**106**
Total deceased donors	**248**	**220**	**237**	**273**	**291**	**265**	**276**	**263**	**321**	**320**	**306**	**282**	**315**

Figure 1: Utilized deceased organ donors in Belgium (2003-2015) [4]

We used the medical record review data from 43,389 patients who died in Belgian critical care units, registered in the Donor Action database between 2010 and 2014, to measure whether the potential was adequately converted to donation (Table 2).

On a total of 43,389 patients, 2676 or 6.2% of all ICU deaths had no contraindications for donation, fulfilled the criteria of a brain death diagnosis and hence were considered as a potential DBD. Average conversion rate of potential into utilized DBD was 41.7 ± 2.1% which showed that in the study cohort 58.3 ± 2.1% of the patients without contraindications, fulfilling the criteria of a brain death diagnosis, were missed along the DBD pathway. The main registered reasons were family objection (15.4 ± 1.8%), no identification (12.9 ± 3.3%), medical unsuitability for donation (10.9 ± 0.9%), treatment withdrawal (9.1 ± 3.5%), failed resuscitation (2.7 ± 0.4%), patient objection (2.4 ± 1.3%) and coroner objection (1.5 ± 0.3%). The reasons of family objection could not be registered in Donor Action.

During the study period, 3520 ventilated patients were considered as a potential DCD whenever the patient was compatible with organ donation on admission and, additionally, the following criteria were met: age ≤ 70 years, absence of sepsis, multiple organ failure or cancer other than brain tumor as cause of death and entrance to a hospital with a DCD program. Average conversion rate of potential into utilized donors was 7.9 ± 0.9%. This showed that 92.1 ± 0.9% of the potential DCD were missed along the DCD pathway. The main registered reasons were lack of identification (24.6 ± 1.8%), medical unsuitability for donation (24 ± 3.2%), family objection (4.0 ± 1.2%) and logistical problems (2.8 ± 0.8%).

Table 2: DBD and DCD pathway in Belgium

	2010 (as % of potential)	2011 (as % of potential)	2012 (as % of potential)	2013 (as % of potential)	2014 (as % of potential)	Total (as % of potential)	SD
Number of deaths on ICU	8384	8646	9190	9331	7838	43,389	
DBD in Belgium							
Preconditions for brain death (after exclusion of contraindications)	772	832	809	823	685	3921	
Signs of severe brain damage	726	801	762	788	662	3739	
Potential DBD: patients who fulfill the criteria of brain death	513	566	561	562	474	2676	
Legal declaration of death	351 (68.4)	418 (73.9)	416 (74.2)	392 (69.8)	358 (75.5)	1935 (72.3)	3.1
Referral to transplant center	268 (52.2)	334 (59.0)	330 (58.8)	296 (52.7)	260 (54.9)	1488 (55.6)	3.3
Utilized DBD	**206 (40.2)**	**253 (44.7)**	**242 (43.1)**	**227 (40.4)**	**189 (39.9)**	**1117 (41.7)**	**2.1**
Reasons for no DBD							
Coroner objection	8 (1.6)	11 (1.9)	8 (1.4)	6 (1.1)	6 (1.3)	39 (1.5)	0.3
Failed resuscitation	16 (3.1)	12 (2.1)	15 (2.7)	18 (3.2)	12 (2.5)	73 (2.7)	0.4
Family objection	75 (14.6)	79 (14.0)	77 (13.7)	98 (17.4)	82 (17.3)	411 (15.4)	1.8
Logistical problems	1 (0.2)	4 (0.7)	0 (0.0)	5 (0.9)	5 (1.1)	15 (0.6)	0.5
Maintenance problems	0 (0.0)	1 (0.2)	2 (0.4)	0 (0.0)	1 (0.2)	4 (0.1)	0.2
Medical unsuitability for donation	50 (9.7)	59 (10.4)	65 (11.6)	60 (10.7)	57 (12.0)	291 (10.9)	0.9

No identification	68 (13.3)	66 (11.7)	95 (16.9)	79 (14.1)	38 (8.0)	346 (12.9)	3.3
Patient objection	9 (1.8)	15 (2.7)	7 (1.2)	12 (2.1)	22 (4.6)	65 (2.4)	1.3
Technical problems	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	3 (0.1)	0.1
Treatment withdrawal	78 (15.2)	47 (8.3)	33 (5.9)	46 (8.2)	40 (8.4)	244 (9.1)	3.5
Other	1 (0.2)	19 (3.4)	16 (2.9)	11 (2.0)	21 (4.4)	68 (2.5)	1.6
Total	**307 (59.8)**	**313 (55.3)**	**319 (56.9)**	**335 (59.6)**	**285 (60.1)**	**1559 (58.3)**	**2.1**
DCD in Belgium							
Potential DCD in all hospitals	1064	1204	1177	1125	1016	5586	
Potential DCD in hospital with DCD program	642	713	758	726	681	3520	
Referral to transplant center	78 (12.1)	112 (15.7)	166 (21.9)	129 (17.8)	140 (20.6)	625 (17.8)	3.9
Utilized DCD	**45 (7.0)**	**50 (7.0)**	**68 (9.0)**	**57 (7.9)**	**59 (8.7)**	**279 (7.9)**	**0.9**
Reasons for no DCD							
Coroner objection	1 (0.2)	6 (0.8)	7 (0.9)	6 (0.8)	7 (1.0)	27 (0.8)	0.3
Failed resuscitation	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.0)	0.1
Family objection	14 (2.2)	37 (5.2)	33 (4.4)	24 (3.3)	33 (4.8)	141 (4.0)	1.2
Logistical problems	26 (4.0)	13 (1.8)	19 (2.5)	18 (2.5)	22 (3.2)	98 (2.8)	0.8
Medical unsuitability for donation	184 (28.7)	185 (25.9)	161 (21.2)	169 (23.3)	145 (21.3)	844 (24.0)	3.2
No identification	148 (23.1)	167 (23.4)	197 (26.0)	196 (27.0)	159 (23.3)	867 (24.6)	1.8
Patient objection	6 (0.9)	5 (0.7)	5 (0.7)	5 (0.7)	7 (1.0)	28 (0.8)	0.2
Technical problems	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.3)	1 (0.1)	3 (0.1)	0.1

Treatment withdrawal	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	1 (0.0)	0.1
Other	218 (34.0)	250 (35.1)	267 (35.2)	249 (34.3)	247 (36.3)	1231 (35.0)	0.9
Total	**597 (93.0)**	**663 (93.0)**	**690 (91.0)**	**669 (92.1)**	**622 (91.3)**	**3241 (92.1)**	**0.9**

Notes: Patients with preconditions for brain death: patients with a severe brain injury where clinical triggers are registered in the medical records, for example Glasgow Coma Scale < 5, no cornea reflex, no pupil reflex…; DBD: donation after brain death; DCD: donation after circulatory death.

In spite of favorable donor rates in Belgium, conversation rates of 41.7 ± 2.1% for DBD and 7.9 ± 0.9% for DCD indicate room for further improvement through optimization of donor detection, family approach and donor management as well as referral of potential donors to a transplant center. Organ procurement organizations in the USA aim to achieve a donor conversation rate for DBD of at least 75% [29]. However, using the parameter of donor conversation rate has also practical limitations, because no uniform definition of a potential organ donor is used in Belgium [30]. As an essential element in striving for self-sufficiency, Belgium should further expand controlled DCD programs into hospitals without a program [31-33]. Their implementation however should avoid the premature referral of potential DBD (before brain death occurs) as DCD, because DBD are more likely to donate multiple transplantable organs [27]. To support the implementation of DCD programs in hospitals, a national protocol is under development, but still under review by the government and in the meantime not available nor published [24].

Legislation on deceased organ donation

At present two types of consent to donation from deceased donors can be distinguished in national legislations: the principle of presumed consent or ‘opting-out’ and explicit consent or ‘opting-in’ [12]. The term ‘opting-out’ may be preferred to ‘presumed consent’ because consent is an active process and cannot be assumed [34]. In Belgium, organ donation and transplantation is regulated by the law of 13 June 1986, which installed an opting-out system. Every mentally

competent person registered in the Belgian population register (or in the foreigner's register for at least six months) is considered as a potential donor after death unless refusal has been explicitly expressed. Previous formal objection or consent can be registered in the national register, to be consulted by the physician through a transplant coordinator prior to organ donation. Informal objection can be expressed in any other way, as long as the physician is notified about it [35]. However, similar to almost all European countries, in daily practice health care professionals are always informing the relatives about organ donation despite the opting-out legal framework [12]. Recent amendments to this act were made in 2012 in accordance to the European directive 2010/45/EU. These amendments relate to standards of quality and safety of the organs, as well as their traceability [36].

To safeguard the wishes of the deceased but in contrast to the previous regulations, a recent amendment [36] imposes a legal requirement to the physician considering organ retrieval to actively inquire about a possible objection for donation expressed by the potential donor. Misinterpretation of this amendment led to the conviction that consent of next of the kin was absolutely needed for proceeding to organ retrieval. This could undermine the highly successful opting-out principle, which was certainly not the goal of this law of 3 July 2012.

After the communication to the family and acceptance of the diagnosis of brain death in DBD or that life-sustaining therapies have become futile in DCD, the physician can state the intention to retrieve organs. At this occasion he/she can ask the family if they know of an eventual objection expressed by the potential donor during his mentally competent life. The proper opinion of the family on organ donation does not matter. This approach clearly differs from an explicit solicitation of agreement by the family, eventually overruling the wishes of the deceased. In practice, it is not always easy to obtain this objective information about the potential donor. Hence, it remains very subjective and dependent on how the family is approached. In the absence of any controllable physical evidence left behind by the deceased, the family can effectively veto

donation and in practice such an objection will always be respected. Any option registered in the national registry however cannot be overruled by the family.

We suggest to describe this amendment in more detail in order to avoid misinterpretations. This should ensure that the right information is given and the approach is consistent with the law. In addition, several questions should be answered such as the time frame of this informative act or the possibility for the physician to delegate this step to a specialized care professional who is trained for this act, such as a donor coordinator, a psychologist or a social worker.

Registration

Every citizen has the possibility to register an agreement or objection to organ or tissue donation at the town hall. An objection does not allow for any differentiation, as it implies an objection against any removal of organs and tissues. To reduce the number of possible objections and in accordance with the right of self-determination, we suggest to offer a differentiated choice, detailing the organs and tissues for which an objection to donation is expressed [37, 38]. To guarantee that a citizen can make a well-informed choice, we suggest that the registration can be carried out by their primary care physician who is also best suited to assess the mental competence of the citizen. Further research should be performed to evaluate the impact of a differentiated choice on donor rates or other factors. As a result of the national awareness campaign [22], since 2014 positive registrations (229,607 at 03/2016) exceed negative registrations (189,271 at 03/2016). Despite this positive trend, these numbers are only representing 3.8% of the total population and will not impact directly on the donor numbers (Figure 2) [39].

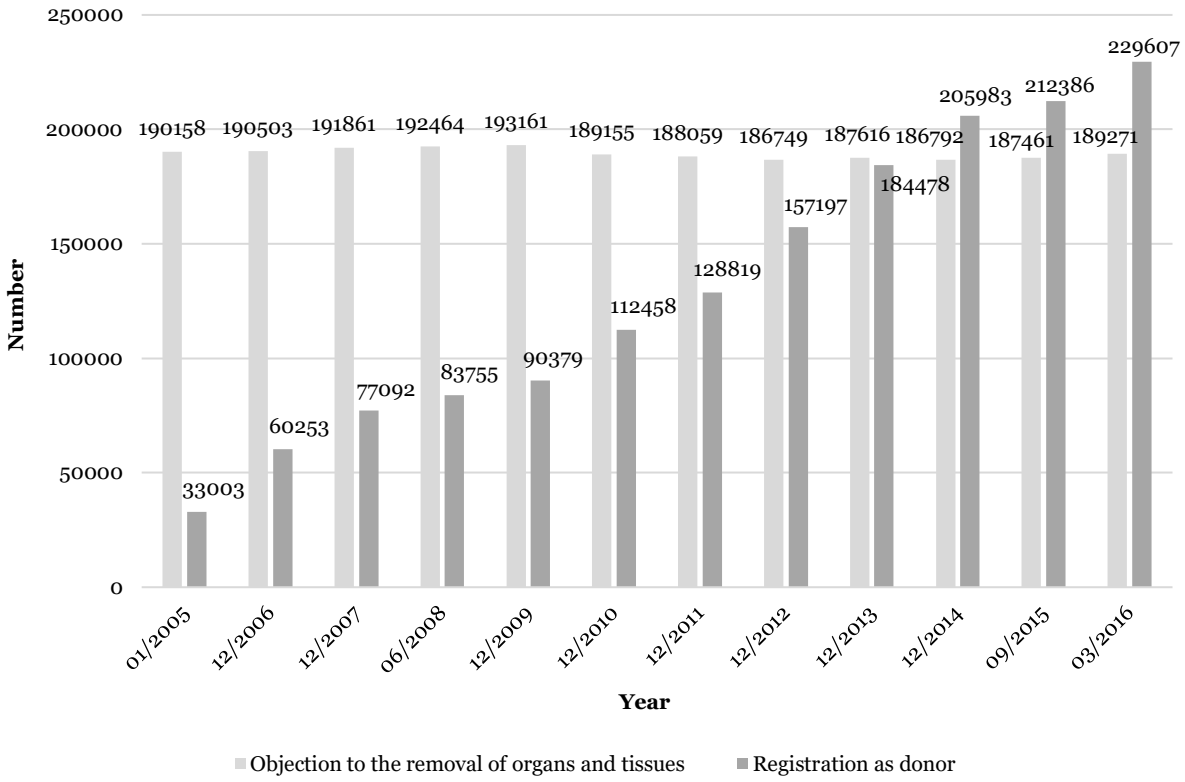


Figure 2: Evolution of registrations in the Belgian national register (2005-2016) [39]

Donor coordination function

The donor coordination function is essential to identify and support all steps in the donation process. This function has been widely recognized, as key to improve not only the effectiveness of the process of donation and transplantation, but also the quality and safety of the organs to be transplanted. This is supported at the EU level through the European directive 2010/45/EU [9, 10]. In accordance with this directive, the Belgian royal decree of 10 November 2012 lays down the norms to be fulfilled by this local donor coordination function. It stipulates that each general hospital, with a recognized intensive and emergency care unit, should have a recognized function of donor coordination, when organ retrieval from deceased donors takes places. This function should be performed by a multidisciplinary team consisting of at least one nurse and one specialist physician with a special professional title in intensive care. One physician and nurse in this team are responsible for the coordination of this team. An intensivist

in this team must be permanently on call and able to be present in the hospital within 15 min. [40]. For many small hospitals with one or two intensivists this is a hurdle because 24/7 attendance cannot be ensured. These hospitals, many of which offered donors in the past, are now excluded from this possibility, as there is no legal framework. Further improvements could be the adaptation of the normative framework to also include hospitals without a 24-h permanence of an intensivist.

Financial reimbursement

For deceased donation, financial reimbursement of organ donation is regulated by the Belgian national health care system. Donor hospitals receive a budget for the operating costs of the donor coordination function [41]. Besides, they receive a conditional financial support for each procured and transplanted organ to cover the medical, pharmaceutical, and hospital costs needed for the characterization and clinical stabilization of the donor. As such, the relatives of a potential DBD should not have to pay further expenses after declaration of brain death. The procurement team also receives a financial support for each organ used for transplantation. The transplant team receives a financial support for the organization of the transplantation.

This conditional financial support also covers the costs for the characterization and clinical stabilization of a DCD. But in contrast with DBD, where it is well formulated that this support covers the costs after declaration of brain death and the family is exempted from any further costs, this is not described for DCD. For potential DCD it remains unclear at what point the relatives are exempted of further expenses. It would be logical to consider this exemption from the time point of first discussion of the option for DCD with relatives of the potential DCD patient onward and to apply the exemption following effective DCD conversion.

Introduction of quality indicators for organ donation (e.g. number of donors converted/absolute number of potential donors detected) could be (partially)

linked to performance-based financing of the donor coordination function, the intensive care unit, an additional intensive care bed, etc. It is likely to be more influential for donor and organ yield than any other measure, but potential disadvantages should be identified. This approach may actually encroach on the delicate balance between respect of the death donor rule [25], by which patients may only become donors after death on the one hand, and perception or reality of overemphasis on organ recovery by health care professionals on the other hand. Hence, this financial incentive carries a risk of perception of overzealousness and of organ recovery causing a donor's death and could undermine public trust in organ donation and transplantation.

Educational and training programs

Further educational training of critical care staff is a key to achieving optimal donation performance. These courses aim both at improving knowledge about donation and transplantation as well as changing attitudes toward transplantation [42]. A number of education and training programs were introduced several years ago in Europe. The European Donor Hospital Education Program (EDHEP), a Eurotransplant initiative launched in 1991, is still running and designed to meet the training needs of critical care staff in breaking bad news, caring for the bereaved and requesting donation [43]. This program aims at improving the communication with donor relatives regarding death and donation by providing insight in the grieving process and relatives' emotional reactions related to the donation procedure [44]. The European Training Program on Organ Donation (ETPOD), supported by the European Union, ended in 2009 and was an initiative that aimed at solving the lack of advanced training programs in the field of organ donation. This program covered different educational levels, from basic knowledge among health care professionals, to specialized training for donor coordinators and hospital managers. A prospective intervention study was performed in 25 target areas with active donor programs from 17 European countries between 2007 and 2009. The number of utilized DBD in the target areas increased from 15.7±14.3 (95% CI: 9.8-21.6) in January-June 2007 (survey S1) to 20.0±17.1 (95% CI: 13-27.1) in January-June 2009 (survey S2) (p = 0.014)

and the number of organs recovered increased from 49.7±48.5 (95% CI: 29.6-69.7) in S1 to 59.3±52.1 (95% CI: 37.8-80.8) in S2 (p = 0.044) after the implementation of the training program. Through this project the educational needs of health care professionals were mapped and high-quality educational materials were created [45].

In Belgium, educational initiatives on a national level include an annual GIFT symposium and regional initiatives with different symposia organized by individual transplant centers. In addition, the government supports EDHEP as a one-day training program for nurses and physicians. This program was attended in 2013/2014 by 273 health professionals: 90.5% nurses (n = 247) and only 9.5% (n = 26) physicians (annual report of 2013 and 2014 received from MVDV & DVD). Further government investments should focus on more specialist-oriented training programs (e.g. based on ETPOD), particularly of donor coordinators, and the implementation of a structured professional network that incorporates continuous training and performance assessment [46]. Obviously, such an assessment can have a discouraging effect on donor coordinators. Beside the critical care staff, Coucke et al. [47] indicated the need for a special focus on primary care physicians who also want to take up their role in the organ donation and transplantation process in Belgium. This study revealed deficits in the knowledge about brain death and the need for training in the field of organ donation and transplantation, to be achieved through specific courses for medical students and postgraduate training of every primary care physician [47].

Donor detection

According to our study of the Donor Action database, 12.9 ± 3.3% of the potential DBD and 24.6 ± 1.8% of the potential DCD were not identified in 2010-2014 in Belgium. The underlying causes are yet to be identified. As far as DCD III is concerned, this procedure is 'younger' and ICU health care professionals should still become acquainted that DCD III may be part of the end-of-life-care process. In Belgium, organ donation mainly runs in low-volume hospitals. There are 98 of a total of 105 acute care hospitals participating in the GIFT project with only 6

hospitals in 2012/2013 having > 10 donors, 9 hospitals with 6-10 donors, 16 hospitals with 3-5 donors, and 67 hospitals with < 3 donors per year (Donor Action data received from CH). Because the majority of the Belgian hospitals have less than three donors per year, another hypothesis can be that health care professionals are rarely confronted with their detection.

To improve the detection, a donor coordinator can install a proactive donor detection protocol inside or outside the ICU, which ensures that a potential donor is detected in a timely manner. This is also defined by the law, as one of the tasks of a donor coordinator, namely to develop a common protocol for the intensive care and emergency units on the management of a potential donor [40]. This potential donor pool may also be extended by sharing the protocol with coronary care or stroke units, as the admission of potential donors is not restricted to ICU or emergency units.

Uniform definitions should be used to ensure a standardized methodology for detection. Recently, there has been a consensus on a universal definition of a possible or potential deceased organ donor. In this critical pathway for organ donation, the progression is described from a possible to a utilized deceased organ donor. As described by Dominguez-Gil et al., this pathway can provide a tool for prospective identification and referral of a possible donor [25]. In order to identify potential donors, the NICE (National Institute for Health and Clinical Excellence) guideline about 'Organ donation for transplantation: improving donor identification and consent rates for deceased organ donation' recommends that UK health care professionals should introduce a system of using clinical triggers for impending brain death. These clinical triggers apply to catastrophic brain injury and include absence of one or more cranial nerve reflexes and a Glasgow Coma Scale (GCS) of 4 or less that is not explained by sedation [48]. These triggers aim to define a standardized point of referral and observational studies demonstrate a statistical increase in the identification of potential donors when used to screen all intensive care patients [49, 50]. Since these are sensitive criteria, less potential donors will be missed, but on the other hand, a substantial proportion of these patients will not die or reach the status of DBD. Consensus

has to be reached which clinical triggers can be used in the Belgian acute hospitals.

Practice clinical guidance

In contrast with other countries, donor coordinators in Belgium have no national reference guidance to a number of critical items, such as identification of potential deceased donors, the approach of family, clinical stabilization of the patient, referral, characterization of the donor and organs, traceability, registration of adverse events and reactions within the existing legal framework. Therefore, they use the guidelines or protocols of the different transplant centers in Belgium. Most of these have been developed within one center over decades, which results in significant variability in the deceased donation process. To establish and maintain a framework for quality and safety that covers all stages of the chain from donation to transplantation, advocated by the Directive [9], further government investments should go to providing evidence-based and best practice guidance at a national level. According to the law, the development of guidelines is shifted to a local level as one of the tasks of the committee of a collaboration association for procurement and transplantation of organs. This collaboration association should exist of health care professionals of at least the following categories: local donor coordination functions; transplant centers; care programs 'heart and heart/lung transplantation' T; emergency care functions; intensive care functions; clinical biology laboratories where HLA tests are conducted; centers for the treatment of chronic renal failure [51].

At a national level, guidance can consist of evidence-based statements that assist clinical decision-making (clinical guidelines), statements of intent (policy) and the articulation of national standards against which practice can be benchmarked. Implementation tools such as protocols, algorithms, or checklists should be promoted to support the guidance implementation in donor hospitals. Care pathways and bundles of care can be used [52]. The federal government currently supports an implementation study which focuses on the development and standardization of the clinical content of a care pathway for organ donation

after brain death, together with a set of indicators to investigate the effectiveness of this care pathway. Because of the lack of well-conducted clinical trials, most of the recommendations in the literature concerning the organ donation process are weakly supported, with most evidence based on surrogate outcomes and retrospective data [53, 54]. Therefore, with the support of the Belgian Transplantation Society and the Belgian Society of Intensive Care Medicine, a Delphi investigation will be conducted by a panel of Belgian experts to gather consensus about the interventions which should be included in this care pathway.

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Chapter 7

Discussion and future perspectives

7. Discussion and future perspectives

Main findings

This doctoral thesis examined different research questions regarding the recommended care for potential donors after brain death and adherence to guidelines in this setting in Belgian intensive care units. The aims were (1) to investigate the impact of existing care pathways for donation after brain death on the quality of care, (2) to identify and select a set of relevant key interventions and quality indicators in order to develop a specific care pathway for donation after brain death and to rigorously evaluate its impact, (3) to assess adherence to these key interventions for the management of potential donors after brain death in a perspective of organ donation in Belgian hospital intensive care units and (4) to define recommendations for further improvement of the deceased organ donation process up to organ procurement in Belgium.

In this chapter, main research findings will first be highlighted, interpreted and integrated. Secondly, recommendations for further improvement of the deceased organ donation process will be discussed. Thirdly, strengths and limitations will be discussed, followed by the practical implications and future perspectives. Finally, overall conclusions of the doctoral thesis will be presented.

Impact of care pathways for donation after brain death

In **chapter 3**, a systematic literature review was conducted to explore the effects of existing care pathways for donation after brain death on the quality of care, identified only one pertinent study [1]. The concerned study was carried out in the United States and examined brain death donors from 88 intensive care units in ten organ procurement organizations managed under the critical pathway and compared them to retrospective data collected at the same participating units. The data showed a significant ($p < 0.01$) increase in the number of organs procured (10.3%) and transplanted (11.3%) per donor when compared to a

historical control group without any reduction in the quality of the transplanted organs [2]. Our systematic review demonstrates a lack of evidence on the use of care pathways in spite of their possible need. As such, further research should focus on the development and standardization of the clinical content of a care pathway for donation after brain death and the identification of quality indicators. These should be used in a prospective effectiveness assessment of the proposed pathway [1].

Key interventions for the management of an adult potential donor after brain death

In **chapter 4**, a set of 65 key interventions was developed based on literature and a RAND modified Delphi study with 18 Belgian experts in the field. Key interventions are those which are required to guarantee high quality care, and hence in this setting will have a significant impact on patient, donor family, recipient or graft outcomes. These key interventions were categorised into ten domains: (I) detection outside the ICU and communication to the ICU (n = 1); (II) detection inside the ICU and notification to a transplant center (n = 12); (III) donor evaluation and characterization (n = 15); donor management: (IV) general care (n = 4), (V) monitoring (n = 14), (VI) cardiovascular management (n = 4), (VII) respiratory management (n = 4), (VIII) renal and electrolyte management (n = 5), (IX) hormone substitution (n = 1); and (X) post procurement care (n = 5). These key interventions are to be considered as a first description of a standard bundle of care for an adult potential donor after brain death and can be included in a care pathway for donation after brain death [3].

Quality indicators for the management of an adult potential donor after brain death

In **chapter 4**, a set of 11 quality indicators (4 structure, 5 process and 2 outcome indicators) were validated for the attributes relevance and feasibility after literature review and the same RAND modified Delphi study. These quality indicators can be used to assess the quality of care for adult potential donors after

brain death and the impact of a care pathway for donation after brain death. Detection of all potential donors after brain death in the intensive care unit and documentation of cause of no donation were rated as the most important quality indicators. Reliability and feasibility in practice of this indicator set needs to be tested in both low- and high-volume donor hospitals. With these indicators, donor coordinators could evaluate the quality of the organ donation process at the hospital level [3].

Adherence to guidelines for the management of organ donors after brain death

In **chapter 5**, we assessed guideline adherence to an expert panel predefined care set in management of a potential donor after brain death in a observational, cross-sectional multicenter study in 21 Belgian ICUs. A retrospective review of 296 patient records of adult utilized donors after brain death used 67 key interventions to describe adherence to guidelines [4].

Overall, adherence to guidelines is moderate, leaving room for improvement. The association with the expert panel ratings of importance was visualized by an importance-performance analysis and showed that there is a research-practice gap. In our study, 19 of the 54 high level of importance key interventions were performed for ≤ 75% of the patients and can thus be classified as high priority interventions to improve the management of a potential donor after brain death (Table 1). Eleven of these underused key interventions did not achieve a threshold performance of 50%. However, inadequate documentation proved an important issue, hampering true guideline adherence assessment. Adherence ranged between 3 and 100% for single key intervention items and on average, patients received 72% of the integrated expert panel recommended care set [4].

Table 1: High priority interventions to improve the management of a potential donor after brain death

Number	Intervention	Performance rate n/N (%)	Not documented n/N (%)	Expert consensus rate (%) [3]
	Detection inside the ICU and notification to a transplant center			
1	Notification to the local donor coordinator at the time these criteria are met.	147/296 (50%)	148/296 (50%)	94%
2	Family approach (bad news conversation and support).	341/586 (58%) [a]	243/586 (41%) [a]	100%
	a) Delivering bad news about the hopeless, medical situation.	198/293 (68%)	95/293 (32%)	
	b) Support of the family (physician, nurse, social assistant, psychologist, pastoral service…).	143/293 (49%)	148/293 (51%)	
3	Information to the family about the diagnosis of brain death.	81/294 (28%)	213/294 (72%)	100%
4	Information to the family about the possibility of organ and tissue donation and the outcome of the National Register.	286/586 (49%) [b]	298/586 (51%) [b]	94%
	a) Information to the family about the possibility of organ and tissue donation.	271/294 (92%)	23/294 (8%)	
	b) Information to the family about the outcome of the National Register.	15/292 (5%)	275/292 (94%)	
	c) Preferably in a separated conversation after family understand the diagnosis of brain death.	34/294 (12%)	258/294 (88%)	
	d) Preferably in a separated conversation after family accept the diagnosis of brain death.	33/294 (11%)	259/294 (88%)	
	Donor evaluation and characterization			
5	Interviewing family and/or other relevant sources to obtain the medical and behavioral history.	68/296 (23%)	223/296 (75%)	89%
6	Clinical examination of the potential donor: written report.	142/296 (48%)	27/296 (9%)	89%
7	Bronchoscopy (on request of the	114/393	23/393	78%

	transplant center, all the following interventions are not always necessary)	(29%) [c]	(6%) [c]	
	a) To allow evaluation of a potential lung donor.	57/135 (42%)	7/135 (5%)	
	b) To collect samples for microbiological tests.	39/127 (31%)	6/127 (5%)	
	c) To perform a bilateral bronchoalveolar lavage (BAL) to clear mucous plugs or blood clots that may contribute to impaired oxygenation.	18/131 (14%)	10/131 (8%)	
	Donor management: general care			
8	Prevention of hypothermia.	93/146 (64%)	28/146 (19%)	78%
	Donor management: monitoring			
9	Monitoring of the core body temperature.	207/296 (70%)	58/296 (20%)	100%
10	New 12-lead ECG for a potential heart donor if there are subsequent changes in monitored complexes.	6/15 (40%)	1/15 (7%)	83%
11	Bronchial secretion sample for microscopy and culture if secretions are present.	167/242 (69%)	25/242 (10%)	89%
12	Monitoring of urine output (hourly).	157/296 (53%)	1/296 (0%)	89%
	Donor management: cardiovascular management			
13	Treatment of tachycardia.	38/83 (46%)	0/83 (0%)	89%
	Donor management: respiratory management			
14	Installation of a lung protective ventilation.	491/1184 (41%) [d]	148/1184 (13%) [d]	89%
	a) Minimum FiO_2 to obtain a PaO_2 between 80 and 100 mm Hg.	107/296 (36%)	1/296 (0.3%)	
	b) Tidal volume (Vt): 6-8 mL/kg (ideal body weight).	134/296 (45%)	45/296 (15%)	
	c) Plateau pressure: < 30 cm H_2O.	199/296 (67%)	93/296 (31%)	
	d) PEEP (Positive End Expiratory Pressure): 8-10 cm H_2O.	51/296 (17%)	9/296 (3%)	
15	Oral hygiene every 6 h.	125/296 (42%)	29/296 (10%)	89%

	Donor management: renal and electrolyte management			
16	If diabetes insipidus, reviewing of the medical history, urinary and blood sample to exclude secondary polyuria.	18/130 (14%)	111/130 (85%)	100%
	Post procurement			
17	Written report that detection of serious adverse events was performed.	10/296 (3%)	19/296 (6%)	100%
	If a serious adverse event was detected, registration and reporting to the transplant center.	5/6 (83%)	1/6 (17%)	
18	Debriefing about the results of the transplantation.	663/1167 (57%) [e]	361/1167 (31%) [e]	94%
	a) The relatives	182/283 (64%)	96/283 (34%)	
	b) The health care professionals	178/296 (60%)	96/296 (32%)	
	c) The primary care physician	98/293 (70%)	82/296 (28%)	
19	Exclusion of any medical, pharmaceutical or hospital costs after the determination of brain death and legal declaration of death on the hospitalization invoice.	217/296 (73%)	27/296 (9%)	94%

[a] 2 = 2a + 2b, [b] 4 = 4a + 4b, [c] 7 = 7a + 7b + 7c, [d] 14 = 14a + 14b + 14c + 14d, [e] 18 = 18a + 18b + 18c

Recommendations for improvement of the deceased organ donation process in Belgium

In **chapter 6**, the following main recommendations for further improvement of the deceased organ donation process up to organ procurement were elaborated by a Belgian expert panel in a position paper [5].

1. Monitoring of donation activities, practices and outcomes

An auditing model of the deceased donation process should be implemented in the Belgian hospitals which includes a continuous clinical chart review of all deaths in the intensive care units and consists of two phases, an internal and an external audit. This auditing model should be based on a set of quality indicators to assess the organizational structures, clinical procedures and outcomes in donor

hospitals. This offers the opportunity of using benchmarks and best practices guidance. These data should be published in an annual national report to ensure transparency of practices.

2. Donor pool

Quality improvement programs should be implemented, focusing on optimization of donor detection, family approach and donor management as well as referral of all potential donors to a transplant center. Implementation of controlled donation after circulatory death programs into hospitals without a program should be encouraged, while avoiding the premature referral of potential donors after brain death (before brain death occurs) as donors after circulatory death.

3. Legislation on deceased organ donation

The expert panel suggests to describe the legal framework more in detail, in order to avoid misinterpretations, how a physician considering organ retrieval should inquire about a possible objection for donation expressed by the potential donor. In addition, a couple of additional questions should be answered such as the time frame of this informative act or the possibility for the physician to delegate this step to a specialized care professional who is trained for this act, such as a donor coordinator or a psychologist.

4. Registration

An objection in the national register to organ or tissue donation does not allow for any differentiation, as it implies an objection against any removal of organs and tissues. To reduce the number of possible objections and in accordance with the right of self-determination, we suggest to offer a differentiated choice, detailing the organs and tissues for which an objection to donation is expressed.

5. Educational and training programs

Further government investments should focus on more specialist-oriented training programs, particularly of donor and transplant coordinators, and the implementation of a structured professional network that incorporates continuous training and performance assessment.

6. Donor detection

To improve the detection, a donor coordinator should install a proactive donor detection protocol inside or outside the ICU, using uniform definitions and clinical triggers. Since these are sensitive criteria, less potential donors will be missed, but on the other hand, a substantial proportion of these patients will not die or reach the status of a donor after brain death.

7. Practice clinical guidance

To establish and maintain a framework for quality and safety that covers all stages of the chain from donation to transplantation, further government investments should go to providing evidence-based and best practice guidance at a national level. Implementation tools such as protocols, algorithms, or checklists should be promoted to support the guidance implementation in donor hospitals. Care pathways and care bundles can be used.

Strengths and limitations

Throughout the manuscripts, strengths and limitations of each study were acknowledged. These can be summarized as follows:

- The systematic review on the effects of existing care pathways for donation after brain death on the quality of care fulfils all requirements to provide a complete, exhaustive summary of current literature.

- The Delphi study and retrospective study provide results which reflect the Belgian situation, hampering generalizability of findings and recommendations.

- A large sample of patients were included in the retrospective audit of the clinical practice in donation after brain death, allowing for robust findings and conclusions.

- The different studies included recommendations that may prove of interest to different stakeholders in the field of organ donation. Hence, a translation from science to clinical practice and management purposes has been provided.

- Taking this low-volume population and the timeframe of this PhD dissertation into account, no research was performed on the effectiveness of a care pathway for donation after brain death.

Practical implications

The 21 acute Belgian hospitals that participated in the Care Pathway for Donation after Brain Death (CP4DBD) quality improvement research project, set up by the Belgian federal government, received (1) information on the set of key interventions and quality indicators, (2) feedback on their actual organization of the care process (retrospective study) and (3) training in how to develop, implement, evaluate, and follow-up a care pathway based on the seven-phase methodology.

One outcome of this dissertation work is a newly developed set of 65 key interventions and 11 quality indicators for the management of a potential donor after brain death [3]. Firstly, the set of 65 key interventions should be piloted by the multidisciplinary ICU teams. Teams that aim to optimize the care should carefully examine this set. The rationale included for the key interventions will help the donor coordinators to motivate their ICU teams to improve the

performance of the different key interventions. Secondly, the set of 11 quality indicators can be used by the donor coordinators to audit their care process for the management of a potential donor after brain death. In daily practice, we recommend that a subset of quality indicators should be identified for follow-up of the care process. Selection should be performed by primary stakeholders (donor coordinators, ICU team, management, etc.,...) and should be based on the following criteria: (i) knowledge of the daily clinical practice, referring to processes which are sub-optimally performed in the organization and so being targets for improvement; and (ii) the SMART principles, referring to the idea that indicators should be Specific, Measurable, Achievable, Relevant and Time bound [6].

This validated set of quality indicators also provides important opportunities for benchmarking between organizations and best practices guidance [7, 8]. However, some barriers need to be considered. The number of utilized donors on an annual basis in the Belgian donor hospitals varies between 0 and 40 (chapter 5), implying that benchmarking is difficult for low-volume hospitals. Furthermore, hospitals already invest significant time and manpower collecting data according to the law, regarding the number of deceased potential donors, utilized donors, different procured organs, together with the reasons why a potential donor has not become a utilized donor [9]. To realize this, a federal application *GIFT action* was offered to the donor coordinators in 2016 to perform this internal evaluation, but this application still has several shortcomings (e.g. number of deceased potential donors cannot be identified in the database). Initiatives from donor hospitals to collect data regarding the set of quality indicators will tend to overlap with *GIFT action*, implying unnecessary duplication. Therefore, we advise that the set of 11 quality indicators should be taken into account when optimizing *GIFT action*.

In the donor hospitals special attention should go to the detection of all potential donors. According to the medical record data in the Donor Action database, deceased potential donors are still missed along the pathway. Between 2010 and 2014, 12.9 ± 3.3% of the potential donors after brain death and 24.6 ± 1.8% of the potential donors after circulatory death were not identified in Belgium

[5]. This was also emphasized in the Delphi study. The process indicator 'Detection of all potential donors after brain death in the intensive care unit' was rated as one of the most important quality indicators. Detection should be based on defined clinical triggers [3]. Nowadays, the Glasgow Coma Scale (GCS) not explained by sedation, is most commonly used to define triggers for identification of potential donors after brain death, but also the Full Outline of Unresponsiveness (FOUR) score can be used. The FOUR may be preferable since it incorporates the pupillary, corneal, and cough reflexes and spontaneous breathing [10]. An integration of these clinical triggers into the electronic medical records, will create opportunities for the donor coordinators to manage and review the deceased donation processes in their hospital.

Another outcome of this dissertation work are the 19 of the 54 high level of importance key interventions which had a low level of performance (underuse key interventions). The participating hospitals in the CP4DBD quality improvement research project received a detailed feedback report regarding their actual organization of the care process. The findings with regard to the low adherence to clinical practise guidelines in that report, should be priorities for the donor coordinators and their multidisciplinary ICU team. When optimizing and auditing their care process for potential donors after brain death, teams should look into the care pathway strategy to reduce variation in clinical practice and to improve the quality of care. Therefore, all participating hospitals received training on care pathway development and implementation, together with the set of key interventions and quality indicators. Moreover, teams should pay additional attention to the clinical documentation, as for different key interventions this is often sub-optimally performed (chapter 5). Documentation, monitoring, and evaluation of variances and outcomes are essential components of a care pathway [11]. The introduction of a checklist can be a useful tool to support this and to address the proven documentation need in the donation pathway. Growing evidence in several areas of healthcare has supported the introduction of such tools in clinical practice [12-14].

However, there are a range of ways to improve the number and quality of organs available from deceased donors [5]. In addition to this CP4DBD project,

other incentives are needed to motivate the donor hospitals and their ICU teams. Actually the incentives to motivate the donor coordinators are limited. Quality measurements as the quality indicators or the compliance with guideline-based recommendations mentioned in this dissertation, can for example be used in a pay-for-performance (P4P) approach. The implementation of such a P4P program is recently a clear priority for the government in the context of the reform of the Belgian hospital financing. These incentive schemes are increasingly used world-wide to improve health system performance but results of evaluations vary considerably. In fact, the empirical evidence on the effect of payment mechanisms on changing healthcare professional practice is surprisingly weak [15-17]. Nevertheless, the available literature is in agreement about the broad direction of the effects of different payment mechanisms [15]. Pilot projects could pave the way for introduction of such a program in the donor hospitals. Another incentive can be knowledge sharing and cooperation within the field, because most donor hospitals are confronted with the same general problems when developing and implementing quality improvement initiatives. Because this is shifted to a local level, the networks around the Belgian transplant centers, further government investments should focus to organize this on a national level.

Future perspectives

The present results provide added value to the upcoming interest in donor management studies. Though, many questions are still unanswered. Based upon the current findings and a number of limitations, several recommendations for future research may be proposed.

First, policy makers might see this national study as a first step in the right direction to improve the recommended care for potential donors because care pathways are used to standardize care, improve coordination, and optimize outcomes with optimal allocation of resources. This CP4DBD research project focused on the steps before implementation of the complex intervention (feedback, evidence-based key interventions, training on care pathway implementation), including the focus on follow-up by a set of quality indicators.

However, in the context of differences in professional culture and clinical practise, some minor adjustments needed to be made to the set of key interventions and quality indicators. Furthermore, a limitation of this CP4DBD project was that the level of expertise in care pathway development and implementation varied considerably between the different donor hospitals. Not all participating Belgian hospitals were members of the Belgian Dutch Clinical Pathway Network (www.nkp.be). Careful attention with regard to the care pathway development and implementation will be required in order to ensure that the 'same' experiment is performed across all the participating hospitals. In addition, it would be interesting to evaluate to which extent the set of key interventions derived from the clinical practice guidelines are included in the care pathway documents, as well as what the facilitators and barriers are for successful implementation.

Second, organ donation is a relatively rare event. Only 3.2 % (n = 1,396) of the ICU deaths (n = 43,389) between 2010 and 2014 became a utilized donor in Belgium [5]. Rare events in rapidly evolving ICU contexts are not amenable to evidence-based-medicine-type protocol driven care (because rapidly evolving, limited empirical evidence), nor to Big Data-type precision medicine approach (because rare events with limited data compared to rate of change of technology and patient characteristics). Therefore consensus methods, such as a Delphi study, can provide a basis for decision-making and considered action when there is limited evidence or when there are doubts about the applicability of evidence. The issue is not whether consensus methods provide evidence that is as good as other ways of generating evidence, but whether the evidence generated by using such methods is better than no evidence or inapplicable evidence [18, 19]. Therefore we advise to repeat this Delphi study related to organ donation after brain death over the time to include new evidence, and this method can also be applied to organ donation after circulatory death which did not form part of this dissertation. Further research should focus on prospective effectiveness assessment of the proposed pathway, in which larger samples could be included over a longer timeframe.

Third, in addition to the studies in this dissertation, more organ donor related multicenter research is needed worldwide and also in Belgium to assess transplant-related interventions (e.g. medication, devices, donor management protocols or care pathways) to maintain or improve organ quality prior to, during, and following transplantation. Organ donor intervention research presents new challenges to the organ donation and transplantation community because of the ethical questions about who should be considered a human subject in a research study, whose permission and oversight are needed, and how to ensure that such research does not threaten the equitable distribution of a scarce and valuable resource. A recent published report from the National Academies of Sciences, Engineering, and Medicine on the *Opportunities for Organ Donor Intervention Research* examined the ethical, legal, regulatory, policy, and organizational issues relevant to conduct research in the United States involving deceased organ donors [20]. It would be interesting to apply this research to the Belgian setting, i.e. a Belgian multidisciplinary expert panel could provide similar recommendations for Belgian policy makers, researchers, and practitioners to improve research into interventions and to investigate the gaps, barriers, and opportunities for such research. This could, for example, consist of recommendations to create a single (inter)national donor registry including a single set of universal information requirements for organ donors, linked to the data which are already collected in the Eurotransplant database for each donor [21]. This database should of course respect and comply with the General Data Protection Regulation (GDPR).

Conclusion

The implementation of a care pathway for organ donation after brain death could be one possible strategy to standardize the donation process and to optimize outcomes. However, there is a lack on studies that evaluated the impact of care pathways for donation after brain death on the quality of care. Care pathways are primarily developed for high-volume hospital diagnoses and low complexity care processes, for which organ donation after brain death does not qualify.

Using a Delphi approach, a multidisciplinary panel of Belgian experts reached consensus for a set of 65 key interventions and 11 quality indicators in order to develop a care pathway for donation after brain death and to rigorously evaluate its impact.

Adherence to a set of key interventions for the management of a potential donor after brain death proved moderate with substantial room for improvement among Belgian donor hospitals. These findings underscore the need for a strategy to improve implementation and documentation of evidence-based guidelines, for which an importance-performance analysis may prove useful.

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Chapter 8

Summary in English and Dutch

8. Summary in English and Dutch

SUMMARY

Background

Research showed that a substantial degree of variability in practices exists between donor hospitals regarding donor detection, determination of brain death, application of donor management techniques or achievement of donor management goals. One of the possible strategies to standardize the donation process and to optimize outcomes could lie in the implementation of a care pathway. However for targeting the right areas for improvement, adherence to guidelines for the management of a potential donor after brain death, hitherto largely unknown, needs to be assessed.

Aims and methodology

In this thesis, four aims were preconceived:

- To investigate the impact of existing care pathways for donation after brain death on the quality of care through a systematic review.
- To identify and select a set of relevant key interventions and quality indicators in order to develop a specific care pathway for donation after brain death and to rigorously evaluate its impact through a RAND modified Delphi study involving a panel of Belgian experts.
- To assess adherence to these key interventions for the management of potential donors after brain death in Belgian hospital intensive care units through a retrospective review of patient records.
- To define recommendations for further improvement of the deceased organ donation process up to organ procurement in Belgium through a position paper elaborated by a Belgian expert panel.

Results

- There is a lack of studies evaluating the impact of care pathways for donation after brain death on the quality of care. This tool has a potential to improve outcomes but its effectiveness is insufficiently explored regarding the donation process.
- Using a Delphi approach, a multidisciplinary panel of Belgian experts reached consensus for a set of 65 key interventions and 11 quality indicators that could be incorporated into a care pathway to be developed for donation after brain death and to rigorously evaluate its impact.
- Adherence to these key interventions for the management of a potential donor after brain death proved moderate with substantial room for improvement among Belgian donor hospitals. These findings underscore the need for a strategy to improve implementation and documentation of evidence-based guidelines, for which an importance-performance analysis may prove a useful decision tool for prioritizing care activities.
- A Belgian expert panel described in a position paper different issues in the monitoring of donation activities, practices and outcomes; donor pool; legislation on deceased organ donation; registration; financial reimbursement; educational and training programs; donor detection and practice clinical guidance.

Recommendations

- Based on the importance-performance analysis, we recommend that hospitals should focus on the high level of importance key interventions with low performance rates, in order to improve the quality of care.
- Donor coordinators should audit their care process for the management of a potential donor after brain death based on quality measurements.

- Investment in benchmarking of donor hospitals to gauge their successes and pinpoint their shortcomings is needed. This includes, integration of clinical triggers in the electronic medical records to detect potential donors, and new incentives to motivate the donor hospitals and their ICU teams to improve the number and quality of organs available from deceased donors.

SAMENVATTING

Achtergrond

Onderzoek toonde aan dat er tussen de donorziekenhuizen nog steeds een aanzienlijke mate van variabiliteit in de zorg bestaat met betrekking tot het detecteren van potentiële orgaandonoren, het vaststellen van de hersendood, het toepassen van donor managementtechnieken en het bereiken van bepaalde donor management doelstellingen. Eén van de mogelijke strategieën om het donatieproces te standaardiseren en de resultaten te optimaliseren, kan de implementatie van een zorgpad zijn. Echter moet onderzoek zich toeleggen of de richtlijnen voor het management van een potentiële hersendode donor worden nageleefd, om te weten waar er in de praktijk nog ruimte voor verbetering is en wat tot nu toe grotendeels onbekend is.

Doelstellingen en methode

In dit proefschrift werden vier doelstellingen vooropgesteld:

- Het onderzoeken van de impact van bestaande zorgpaden voor donatie na hersendood op de kwaliteit van zorg door middel van een systematisch literatuuronderzoek.

- Het identificeren en selecteren van een set van relevante sleutelinterventies en kwaliteitsindicatoren zodat een zorgpad voor donatie na hersendood kan worden ontwikkeld en de impact ervan grondig kan worden geëvalueerd, door middel van een RAND gemodificeerde Delphi-studie met een panel van Belgische experts.

- Het vaststellen van de naleving van deze sleutelinterventies voor het management van een potentiële hersendode donor in een set van Belgische intensieve zorg afdelingen door middel van een retrospectieve beoordeling van patiëntendossiers.

- Het formuleren van aanbevelingen voor verdere verbetering van het orgaandonatie proces in België bij overleden donoren tot aan de orgaanprelevatie door middel van een beleidspaper opgesteld door een Belgisch experten panel.

Resultaten

- Er is een gebrek aan studies die de impact van zorgpaden voor donatie na hersendood evalueren op de kwaliteit van zorg. Deze methodiek heeft een potentieel om de resultaten te verbeteren, maar de effectiviteit is onvoldoende onderzocht met betrekking tot het donatieproces.
- Met behulp van een Delphi-benadering, bereikte een multidisciplinair panel van Belgische experts een consensus over een reeks van 65 sleutelinterventies en 11 kwaliteitsindicatoren, die kunnen worden opgenomen in een zorgpad voor donatie na hersendood en de impact ervan grondig kunnen evalueren.
- De naleving van deze sleutelinterventies voor het management van een potentiële donor na hersendood was matig, met heel wat ruimte voor verbetering in de Belgische donorziekenhuizen. Deze bevindingen onderstrepen de behoefte ten aanzien van een strategie die de implementatie en documentatie van evidence-based richtlijnen kan verbeteren. Een importance-performance analyse kan hiervoor een nuttig besluitvormingsinstrument zijn voor het prioriteren van zorgactiviteiten.

Aanbevelingen

- Op basis van de importance-performance analyse adviseren wij dat ziekenhuizen zich richten op de belangrijke sleutelinterventies met lage performance, om de kwaliteit van zorg te verbeteren.
- Donorcoördinatoren moeten hun zorgproces auditen voor het management van een potentiële donor na hersendood op basis van kwaliteitsmetingen.

- Investeringen moeten zich focussen op benchmarking van donorziekenhuizen zodat hun successen worden gemeten en hun tekortkomingen worden aangetoond. Dit omvat integratie van klinische triggers in het elektronisch medische dossier om potentiële donoren te detecteren, en nieuwe prikkels om donorziekenhuizen en hun teams op de afdeling intensieve zorg te motiveren zodat het aantal en de kwaliteit van organen beschikbaar van overleden donoren wordt verbeterd.

Chapter 9

Acknowledgements and curriculum vitae

9. Acknowledgements and curriculum vitae

Dankwoord

Iets in mij zegt me dat dit stukje, het dankwoord, het meest gelezen hoofdstuk zal zijn in dit boekje. In tegenstelling tot de voorgaande stukken waar ik mijn verstand liet spreken, laat ik nu mijn hart even aan het woord.

Eerst en vooral wil ik mijn promotor Prof. dr. Koenraad Vandewoude bedanken. Koen, u hebt een passie voor de zorg rond orgaandonatie & -transplantatie en hebt er voor gezorgd dat ik mijn doctoraatsonderzoek kon aanvatten. U liet me ook de ruimte om mijn weg hierin te bewandelen. Bedankt voor uw vertrouwen in mijn kunnen. U was een belangrijke determinant in het slagen van dit project. Ondanks uw drukke agenda, maakte u steeds tijd vrij voor een overlegmoment. Bedankt.

Vervolgens wil ik mijn co-promotor Prof. Dr. Kris Vanhaecht bedanken. Kris, u hebt een belangrijke bijdrage geleverd in het onderzoeksdesign van dit doctoraatsonderzoek. Steeds was u bereikbaar voor overleg en als het ware 'per kerende' kreeg ik respons op mijn e-mails. Uw brainstormsessies hebben me erg gestimuleerd om de zaken vanuit een nieuw perspectief te bekijken, wat zonder twijfel erg heeft bijgedragen tot de kwaliteit van deze doctoraatsthesis. Bedankt.

Een speciaal woord van dank gaat uit naar Prof. Dr. Dirk Vogelaers. Dirk, ook al was u niet mijn promotor, samen met Koen nam u die rol wel mee op. Uw klinische, wetenschappelijke en stimulerende input, samen met uw kritische feedback, waren onontbeerlijk voor de kwaliteit van dit doctoraatsonderzoek. Keer op keer slaagde u erin om de manuscripten naar een hoger niveau te tillen. U hebt er ook voor gezorgd dat ik mijn werkzaamheden kon uitvoeren vanuit de dienst Algemene Inwendige Ziekten. Mijn oprechte dank hiervoor.

Graag wil ik ook de overige leden van de CP4DBD onderzoeksgroep bedanken: Prof. Dr. Eric Hoste, Prof. Dr. Patrick Ferdinande, Prof. Dr. Xavier Rogiers, Prof. Dr. Kristof Eeckloo en Dr. Margareta Haelterman. Bedankt voor de aangename

samenwerking, samen met het advies en ondersteuning gedurende dit doctoraatstraject.

Dank aan de examencommissie om deze doctoraatsthesis kritisch te lezen en te voorzien van opbouwende kritiek.

Aan mijn collega's van de dienst Algemene Inwendige Ziekten (UZ Gent) en de afdeling intensieve zorg (AZ Sint-Lucas Gent), bedankt voor de ondersteuning gedurende het volledige doctoraatsproject. Ik wil jullie bedanken voor de gesprekjes tussendoor, het luisteren, de bemoedigende woorden en de ontspannende momenten. Mijn oprechte dank gaat in het bijzonder uit naar Charlotte, Sophie, Liesbeth, Els, Kjell en Peter.

Graag wil ik ook mijn vrienden en familie bedankten. Dankzij jullie sta ik nu hier. Bedankt ouders, schoonouders, (schoon)broers, (schoon)zussen voor de opvang van de kinderen. Zo gaven jullie me de tijd, en wat rust voor Dorien, om dit werk te voltooien.

Beste ouders, bedankt om in mij te geloven en me alle kansen te geven om mezelf te ontplooien vroeger, nu en in de toekomst. Jullie hebben me de zelfstandigheid en de verantwoordelijkheidszin aangeleverd die ik dagdagelijks heb kunnen gebruiken. Maar vooral een grote dank je wel om een super oma en opa te zijn voor mijn drie grote schatten.

Dorien, jou wil ik bedanken voor jouw steun en houvast doorheen dit hele verhaal. Zonder jou was dit alles niet mogelijk. Je hebt me steeds gestimuleerd om nieuwe uitdagingen op te zoeken. Bedankt om zo een super mama te zijn. En tot slot, mijn drie grote schatten, Aurélie, Amelou en Maribel, dank je wel om me te leren relativeren en te genieten van elkaar. Ik zie jullie heel graag!

Curriculum vitae

PERSONALIA

Name	Pieter Hoste
Nationality	Belgian
Place of birth	Ghent
Date of birth	11 / 08 / 1983
Address	Eendrachtstraat 30 9000 Ghent
Legal cohabitation	Dorien Van Caenegem
Children	Aurélie Hoste - 29/04/2011 Amelou Hoste - 30/10/2012 Maribel Hoste - 14/03/2016
Mobile	+32 494 37 52 27
Email	piehoste.hoste@ugent.be pieter.hoste2@uzgent.be pieter.hoste@azstlucas.be

EDUCATION

- Secondary School
  Course Science and Mathematics (6-hrs mathematics)
  Sint - Lodewijkscollege, Lokeren, 2001

- Bachelor of Nursing
  Arteveldehogeschool, Ghent, 2004

- Bachelor of Intensive and Emergency Care
  Hogeschool Gent, Ghent, 2005

- Postgraduate course in Tropical medicine
  Institute of Tropical Medicine, Antwerp, 2007

- Master of Science in Health Care Management and Policy
  Ghent University, Ghent, 2012

PROFESSIONAL CURRICULUM

Professional experience

- 25 July 2005 - 31 Oct. 2005, General Hospital Sint-Lucas, Ghent
  Midcare nurse

- 1 Nov. 2005 - 31 Aug. 2014, General Hospital Sint-Lucas, Ghent
  Intensive care nurse

- 1 Feb. 2012 - 31 Aug. 2018, General Hospital Sint-Lucas, Ghent
  Donor coordinator

- 1 Sept. 2014 - 31 Aug. 2018, Ghent University, Faculty of Medicine and Health Sciences, Department of Internal Medicine
  PhD student

- 1 Sept. 2014 - 31 May 2019, Ghent University Hospital, Department of General Internal Medicine
  Staff member expert

- 1 Mar. 2016 - 28 Feb. 2017, General Hospital Sint-Lucas, Ghent
  Staff member care program stroke

- 1 Sept. 2018 - present, General Hospital Sint-Lucas, Ghent
  Head nurse operating room

Teaching experience

- Guest lecturer: Bachelor of Intensive and Emergency Care, Hogeschool Gent, 2015 - 2017
  Topic: organ donation & - transplantation

Academic functions

- Lieze Scholberg & Lien Vandenhoeke (co-promotor of master thesis): De variatie in het zorgproces bij orgaandonatie na hersendood (Ugent, 2016 - 2017)

- Eline Wittevrongel (mentor of master thesis): Organ donation after brain death in UZ Leuven (KU Leuven, 2016-2017)

Reviewer Board member

- Reviewer Journal of Critical Care

PUBLICATIONS

Theses

- Thesis Master of Science in Health Care Management and Policy (2012): Ontwikkeling van een zorgpad heart-beating orgaandonatie in het AZ Sint-Lucas Gent.

A1-publications

- Hoste P., Ferdinande P., Hoste E., Vanhaecht K., Rogiers X., Eeckloo K., Van Deynse D., Ledoux D., Vandewoude K. & Vogelaers D. (2016) Recommendations for further improvement of the deceased organ donation process in Belgium. Acta Clinica Belgica 71(5), 303-312.

- Hoste P., Vanhaecht K., Ferdinande P., Rogiers X., Eeckloo K., Blot S., Hoste E., Vogelaers D. & Vandewoude K. (2016) Care pathways for organ donation after brain death: guidance from available literature? Journal of Advanced Nursing 72(10), 2369-2380.

- Hoste P., Hoste E., Ferdinande P., Vandewoude K., Vogelaers D., Van Hecke A., Xavier R., Eeckloo K. & Vanhaecht K. (2018) Development of key interventions and quality indicators for the management of an adult potential donor after brain death: a RAND modified Delphi approach. BMC Health Services Research 18(1), 580.

- Hoste P., Vandewoude K., Delesie L. & Vogelaers D. (2018) Effectiveness of institutional policies, protocols and order sets on organ donation rates in the Intensive Care Unit. Intensive and Critical Care Nursing (49), 79-80.

- Hoste P., Ferdinande P., Vogelaers D., Vanhaecht K., Hoste E., Rogiers X., Eeckloo K. & Vandewoude K. (2019) Adherence to guidelines for the management of donors after brain death. Journal of Critical Care (49), 56-63.

SCIENTIFIC ACTIVITIES

International congresses - oral presentations (submitted abstract)

- Hoste P., Hoste E., Ferdinande P., Vogelaers D., Van Hecke A., Rogiers X., Eeckloo K., Vanhaecht K. & Vandewoude K. (2017) Development of key interventions and quality indicators for the management of an adult potential donor after brain death: a RAND modified Delphi approach. Transplant International 30(suppl. 2), 183. Presented at: 18th congress of the European Society for Organ Transplantation, September 24-27, 2017, Barcelona, Spain.

- Hoste P., Hoste E., Ferdinande P., Vogelaers D., Van Hecke A., Rogiers X., Eeckloo K., Vanhaecht K. & Vandewoude K. (2017) Development of key interventions and quality indicators for the management of an adult potential donor after brain death: a RAND modified Delphi approach. Presented at: Eurotransplant jubilee congress, October 04-06, 2017, Noordwijk, The Netherlands.

International congress - poster presentation

- Hoste P., Hoste E., Ferdinande P., Vogelaers D., Van Hecke A., Rogiers X., Eeckloo K., Vanhaecht K. & Vandewoude K. (2017) Development of key interventions and quality indicators for the management of an adult potential donor after brain death: a RAND modified Delphi approach. Presented at: Eurotransplant jubilee congress, October 04-06, 2017, Noordwijk, The Netherlands.

National congress - oral presentation (submitted abstract)

- Hoste P., Hoste E., Ferdinande P., Vogelaers D., Van Hecke A., Rogiers X., Eeckloo K., Vanhaecht K. & Vandewoude K. (2017) Development of key interventions and quality indicators for the management of an adult potential donor after brain death: a RAND modified Delphi approach.

Presented at: 24th Annual meeting of the Belgian Transplantation Society, March 16-17, 2017, Brussels.

Chapter 10

Information letter and questionnaire used in article

10. Information letter and questionnaire used in article

DONATION AFTER BRAIN DEATH
RAND MODIFIED DELPHI METHOD

Address of correspondence:
piehoste.hoste@ugent.be

Pieter Hoste, RN, MSc[1, 2, 3, 4], Patrick Ferdinande, MD, PhD[5], Kris Vanhaecht, RN, PhD[6, 7, 8], Xavier Rogiers, MD, PhD[2, 9], Kristof Eeckloo, LLM, PhD[2], Eric Hoste, MD, PhD[2, 10, 11], Dirk Vogelaers, MD, PhD[1, 2, 3], Ann Van Hecke, RN, PhD[2, 12, 13, 14] & Koenraad Vandewoude, MD, PhD[2, 3]

[1] Department of General Internal Medicine, Ghent University Hospital, Ghent, Belgium; [2] Faculty of Medicine and Health Sciences, Ghent University, Ghent, Belgium; [3] Department of Internal Medicine, Ghent University, Ghent, Belgium [4] Department of Intensive Care, General Hospital Sint-Lucas, Ghent, Belgium; [5] Surgical and Transplantation ICU, University Hospitals Leuven, Leuven, Belgium; [6] Leuven Institute for Healthcare Policy, Department of Public Health and Primary Care, KU Leuven - University of Leuven, Leuven, Belgium; [7] Department of Quality Management, University Hospitals Leuven, Leuven, Belgium; [8] European Pathway Association, Kapucijnenvoer, Leuven, Belgium; [9] Department of Transplant Surgery, Ghent University Hospital, Ghent, Belgium; [10] Department of Intensive Care Medicine, Ghent University Hospital, Ghent, Belgium; [11] Research Foundation - Flanders (FWO), Egmontstraat, Brussels, Belgium; [12] University Centre for Nursing and Midwifery, Ghent University, Ghent, Belgium; [13] Department of Public Health, Ghent University, Ghent, Belgium; [14] Nursing Department, Ghent University Hospital, Ghent, Belgium.

INFORMATION LETTER

Care pathways, also known as clinical pathways or critical pathways, are used worldwide for a variety of patient groups to reduce undesired variability and standardize care based on the latest evidence. Nonetheless very few methodologically robust prospective studies have been performed and published on the impact of pathways on quality and efficiency of care. Care pathways have also been developed for donation after brain death in order to optimize the donation process. But only the study of Rosendale et al. (2002) has evaluated the impact of such a care pathway. The goal of this study is to select a set of key interventions to be included in a care pathway for donation after brain death as well as a set of quality indicators that are relevant to assess the quality of care for potential donors after brain death (see glossary) and the impact of this care pathway.

For this purpose, we wish to consult a multidisciplinary Delphi panel of physicians and nurses in Belgium in order to guarantee relevance for clinical practice and generalizability of results. We are looking for experts meeting the following requirements: (1) Involvement in the donation process after brain death; (2) Relevant experience (preferably for a minimum of 10 years) in the field of organ donation; (3) A minimum of 3 organ donors throughout 2015 if the expert is working in a donor hospital; (4) Motivation to complete the Delphi task for the whole process to ensure consensus on this set of key interventions and quality indicators.

If you are able and willing to be involved in this Delphi panel, you can send an email to **piehoste.hoste@ugent.be**. An electronic questionnaire will be sent to you. Completion of the questionnaire for each round will take about 45 minutes. After three anonymous rounds (for more details see further on), it may be necessary to organize a physical meeting with the expert panel to discuss points of view. Your judgments and opinions will remain strictly confidential.

The questionnaire is built up in three parts:

Part I: demographic information (only in round 1)

In this part, we would like you to fill in some general information to describe our expert panel.

Part II: selection of key interventions

Based on guidelines [1-10], process flow diagrams [11-19], and review articles [20-27], a list of key interventions starting from an adult patient with a devastating brain injury or lesion with evolution to imminent brain death until post procurement are defined. Key interventions are those which are required to guarantee high quality care, and hence in this setting will have a significant impact on patient, donor family, recipient or graft outcomes. In a first round you can comment on the listed key interventions or add new ones. In a second round, we would like you to indicate on a 9-point rating scale, if the key interventions will contribute to the quality of care for

the management of a potential donor (or the donor family, recipient or graft). In addition, in a third round you will have the possibility to adjust your answers based on the group responses. The aim is to determine the level of consensus about the key interventions which should be included in a care pathway for donation after brain death.

Part III: selection of quality indicators

Based on the results of the ODEQUS project [28] and the guidelines [1-10], process flow diagrams [11-19], and review articles [20-27], a selection of quality indicators for assessing the quality of care are defined. In a first round you can comment on the listed quality indicators or add new ones. In a second round, we would like you to evaluate this set of indicators on relevance and feasibility on a 9-point rating scale. In addition, in a third round you will have the possibility to adjust your answers based on the group responses. The aim is to determine the level of consensus about the indicators which should be used to study the quality of care and the impact of a care pathway for donation after brain death.

We would like to thank you in advance for your effort in helping us with this project. Please do not hesitate to contact us if you have any questions.

QUESTIONNAIRE PART I: DEMOGRAPHIC INFORMATION

1. **Name:** .....
2. **Name of your hospital / organization:** .....
3. **Type of hospital:**

   ☐ Academic hospital

   ☐ Non-academic community hospital

   ☐ Other: .....

4. **Number of intensive care beds in your hospital / organization:** ... **beds**
5. **Number of organ donors after brain death and circulatory death in your hospital / organization:**

   - 2013: .....
   - 2014: .....
   - 2015: .....

6. **Professional group:**

   ☐ Medical doctor

   ☐ Nurse

   ☐ Other: .....

7. **Function (multiple answers possible):**

   ☐ Intensivist

   ☐ Anesthesiologist

   ☐ Urgentist/emergency physician

   ☐ ICU nurse

   ☐ Donor coordinator

   ☐ Transplant coordinator

   ☐ Procurement surgeon

   ☐ Researcher

☐ Government

☐ Other (please specify):

8. Years of experience in organ donation: … years

9. Age:

☐ 20-29 ☐ 30-39 ☐ 40-49 ☐ 50-59 ☐ 60-69 ☐ > 70

10. Sex:

☐ Male ☐ Female

QUESTIONNAIRE PART II: KEY INTERVENTIONS FOR DONATION AFTER BRAIN DEATH (DELPHI ROUND 2)

First round: please comment on the listed key interventions if they are not well formulated for you or add new ones.

For example: key intervention X
Comments on this key intervention: .....
Reference(s): .....

Second & third round: please indicate on a 9-point rating scale, if the key intervention will contribute to the quality of care for the management of the potential donor (or the donor family, recipient or graft), with 1 indicating "strongly disagree" and 9 "strongly agree".

For example: key intervention X

Strongly disagree				Undecided				Strongly agree
1	2	3	4	5	6	7	8	9
☐	☐	☐	☐	☐	☐	☐	☐	☐

Definition of consensus after the third round

A key intervention will be considered valid if it has a median score of 7 or more with 75% of more of the ratings in the highest tertile (Likert score: 7-9).

Detection outside the ICU & communication to the ICU

1. Detection of a patient with a devastating brain injury or lesion with evolution to imminent brain death (for example intracranial hemorrhage, trauma, cerebral ischemia etc.) on a unit outside the ICU (for example emergency services, stroke units, etc.) and early communication of the presence of this patient to the ICU physician (and referral to the ICU).

Detection inside the ICU & notification to a transplant center

2. Detection of a potential donor after brain death inside the ICU.
   Detection should be based on defined clinical triggers in patients who have had a devastating brain injury or lesion, while recognizing that clinical situations vary
   - A Glasgow Coma Scale score of 4 or less that is not explained by sedation and
   - The absence of one or more cranial nerve reflexes

   Unless there is a clear reason why the above clinical triggers are not met and/or a decision has been made to perform brainstem death tests, whichever is the earlier.
3. Notification of the donor coordinator at the time these criteria* are met.
   *A Glasgow Coma Scale (GCS) score of 4 or less that is not explained by sedation and the absence of one or more cranial nerve reflexes.
4. Assessment of the prerequisites prior to the clinical evaluation of brain death:
   - Coma, irreversible, and cause known.
   - Neuroimaging compatible with coma.
   - Central nervous system depressant drug effect absent (if indicated, toxicology screen; if barbiturates given, serum level < 10 μg/mL).
   - No evidence of residual paralytics (electrical stimulation if paralytics used).
   - Absence of severe acid-base, electrolyte, and endocrine abnormality.
   - Normothermia or mild hypothermia (core temperature > 36°C).
   - Systolic blood pressure > 100 mm Hg. Vasopressors may be required.
   - No spontaneous respiration.
5. Approaching the family:
   - Delivering bad news about the hopeless, medical situation.
   - Support of the family (physician, nurse, social assistant, psychologist, pastoral service…).
6. Notification of the potential donor after brain death by an ICU physician to a transplant center:
   - Briefing: name, date of birth, diagnosis & therapy, short medical and behavioral history, etc.
   - Check the medical contra-indications for organ and tissue donation on file with the transplant center.
   - Is there a registration in the National Register, checked by the transplant center?
7. Determination of brain death.
8. Legal declaration of death: registration of time of death and the way in which it is

determined on a dated and signed official report.

9. Notification of legal authorities if the cause of death is unknown or suspicious.
10. Informing the family about the diagnosis of brain death.
11. Informing the family about the outcome of the National Register and the possibility of organ and tissue donation, preferably in a separated conversation after family understand and accept the diagnosis of brain death.
12. Give clear, unambiguous information about the next main steps about the donation process to the relatives.
13. Feedback about the approach of the family and legal authorities (if the cause of death is unknown or suspicious) and discussion about the necessary investigations for donor evaluation and characterization to a transplant center.

Donor evaluation and characterization

14. Interviewing family and/or other relevant sources (e.g. life partner, cohabitant, caretaker, friend or primary care physician) to obtain the medical and behavioral history of the potential donor which might affect the suitability of the organs for transplantation and imply the risk of disease transmission.
15. Reviewing medical charts to obtain the medical and behavioral history of the potential donor which might affect the suitability of the organs for transplantation and imply the risk of disease transmission.
16. Clinical examination of the potential donor.
17. Collect a blood sample and ship it to a transplant center for appropriate blood tests.
18. Discuss with a transplant center, the necessity to examine a blood sample for the determination of ABO, rhesus blood group or additional laboratory tests.
19. Collect a urine sample (if not shipped to a transplant center) for measurement of sediment, protein & glucose.
20. Perform a chest X-ray, mandatory for each potential donor and to allow evaluation of a potential lung and/or heart donor.
21. Discuss with a transplant center, the necessity to perform a bronchoscopy by an experienced physician to allow evaluation of a potential lung donor together with a bilateral bronchoalveolar lavage to collect samples for microbiological tests and to clear mucous plugs or blood clots that may contribute to impaired oxygenation.
22. Perform an arterial blood gas to allow evaluation of a potential lung donor.
23. Discuss with a transplant center, the necessity to perform an arterial blood gas for a potential lung donor after 10 minutes ventilation with FiO_2 100% & 5 cm H_2O PEEP.
24. Perform a 12 lead ECG to allow evaluation of a potential heart donor.
25. Discuss with a transplant center, the necessity to perform a cardiac ultrasound by an experienced physician to allow evaluation of a potential heart donor.
26. Discuss with a transplant center, the necessity to perform, if possible, a coronary angiography if cardiac ultrasound is acceptable but other comorbidities are present.
27. Discuss with a transplant center, the necessity to perform an abdominal ultrasound (or CT

scan) to allow evaluation of a potential liver, pancreas and/or kidney donor.

28. Collect the minimum data, as requested by the transplant center for the characterization of organs and donor, on a donor information form and send it together with the results of the investigations to a transplant center.

Donor management: general care

29. Provide at least an arterial line and a central venous line, if not present.
30. Continue enteral feeding until otherwise instructed by the transplant center.
31. Continue appropriate antibiotic therapy and other life supporting pharmacotherapy, only if indicated.
32. Continue an appropriate prescription of deep venous thrombosis prophylaxis (low molecular weight heparin).
33. Ensuring a prescription of low-dose dopamine with a dose of (and not exceeding) 4 µg/kg/min until the aortic clamping and halve the dosage or terminate the infusion earlier when circulatory adverse effects occurred in association with the dopamine infusion, such as tachycardia (> 120 beats per min) or a marked increase in blood pressure (MAP > 110 mm Hg).
34. Use warming mattress, blankets or warmed intravenous fluids if needed, to prophylactically prevent hypothermia.
35. Reduce vasopressors (if possible) while maintaining hemodynamic stability.

Donor management: monitoring

36. Monitor the core body temperature.
    Target temperature: between 35-37°C.
37. ECG monitoring of heart rate.
    Target heart rate between 60-100 beats per minute.
38. Repeat a 12-lead ECG for a potential heart donor if there are subsequent changes in monitored complexes.
39. Invasive arterial pressure monitoring.
    Target mean arterial pressure: ≥ 60 mm Hg.
40. Measure additional parameters with extended monitoring in case of a patient with hemodynamic instability, by using for instance a pulmonary artery catheter, PiCCO or oesophageal Doppler.
41. Measure additional parameters with extended monitoring in case of a patient with hemodynamic instability, by using transthoracic or transoesophageal echocardiography.
    Target ejection fraction: ≥ 50 %.
42. Ensuring a recent chest X-ray examination for a potential lung and/or heart donor is available.
43. Monitoring of ventilator parameters.
44. Periodically re-assess cuff pressure to check if there is no cuff leak and if cuff pressure is between 20-30 cm H_2O to avoid aspiration.
45. Peripheral oxygen saturation monitoring (SaO_2).

Target SaO_2: > 95 %.

46. Perform a blood gas analysis on a regular basis.
    Target pH: 7.3-7.5.
    Target arterial oxygen tension (PaO_2): 80-100 mm Hg.
    Target arterial carbon dioxide tension ($PaCO_2$): 35-45 mm Hg.
47. Send a bronchial secretion sample for microscopy and culture if secretions are present.
48. Perform a bronchoscopy for diagnosis or therapy if clinically indicated.
49. Estimate the effective intravascular volume and overall fluid status by chart review and clinical examination.
50. Monitor hourly urine output, particularly looking for any suggestion of the onset of diabetes insipidus (polyuria).
    Target urine output: 0.5-3 mL/kg/h.
51. Measure blood electrolytes on a regular basis.
    Target serum sodium: ≤ 155 mEq/L.
52. Monitoring of glycemic status.
    Target blood glucose: ≤ 180 mg/dL.
53. Measure routine full blood counts to examine the need for transfusion of red blood cells if clinically indicated.
    Target hemoglobin: > 7 g/dL.
54. Ensuring coagulation screening or thromboelastography to target therapy if there is a clinically relevant bleeding.

Donor management: cardiovascular management (hypotension)

55. Treat the systemic arterial hypertension related to "adrenergic storm" of severe degree (MAP > 120 mm Hg) and prolonged (> 30 to 60 minutes) with calcium entry blockers or short-acting cardioselective beta-blockers.
56. Use isotonic crystalloids for intravascular volume replacement and use blood products and colloids (albumin) for specific circumstances.
57. Avoid hydroxyethyl starch (HES) for intravascular volume replacement.
58. Ensuring an appropriate prescription of vasoactive drugs when correction of the volume deficit fails to achieve the threshold hemodynamic goals.

Donor management: cardiovascular management (bradycardia)

59. Treat bradycardia causing hemodynamic instability, with a short acting β-adrenergic agonist (epinephrine/dopamine/dobutamine/isoprenaline) or occasionally transvenous pacing. Don't use atropine because bradycardia are the consequence of high-level vagal stimulation and exhibit a high degree of resistance to atropine.

Donor management: cardiovascular management (tachycardia)

60. Treat tachycardia by following the established advanced cardiopulmonary life support guidelines.

Donor management: respiratory management

61. Ensuring a lung protective ventilation is installed:

- Minimum FiO_2 to obtain a PO_2 between 80-100 mm Hg
- Tidal volume (Vt): 6-8 mL/kg (ideal body weight)
- Plateau pressure: < 30 cm H_2O
- PEEP (Positive End Expiratory Pressure): 8-10 cm H_2O

62. Maintain 30-45° head of bed elevation to avoid aspiration.
63. Perform recruitment maneuvers and repeat when indicated.
64. Perform intermittent nasopharyngeal suction.
65. Perform intermittent tracheal suction, by preference using a closed circuit.
66. Apply a prescription of oral hygiene every 6 hours.

Donor management: renal and electrolyte management (oliguria < 0.5 mL/kg/h)

67. Treat hypovolemia, hypotension and cardiac dysfunction and consider diuretic only if needed.

Donor management: renal and electrolyte management (polyuria > 3 mL/kg/h)

68. Review the medical history, urinary and blood sample to exclude secondary polyuria: osmotic (Mannitol, hyperglycemia), induced (diuretic) or adapted (fluid overload).
69. Confirm diabetes insipidus: urine specific gravity below 1.005 g/mL or trend towards hypernatremia/hyperosmolarity.
70. Treat diabetes insipidus with sufficient fluid volume replacement to compensate polyuria and anti-diuretic hormone replacement.
    - Fluid volume replacement with monitoring of electrolytes and blood glucose levels.
    - Anti-diuretic hormone replacement with desmopressin as a first line medication.

Donor management: renal and electrolyte management (electrolyte disturbances)

71. Treat electrolyte disturbances.

Donor management: hormone substitution

72. Ensuring a prescription of hydrocortisone to reduce the cumulative dose and administration duration of vasopressors: hydrocortisone 50 mg + continuous infusion of 10 mg/h until the aortic clamping.
73. Ensuring a prescription of methylprednisolone for a potential liver donor: 250 mg bolus + 100 mg/hour until recovery of organs.
74. Consider thyroid replacement therapy for hemodynamically unstable donors or for potential heart donors with abnormal (<45%) left ventricular ejection fraction.
75. Ensuring an appropriate prescription of insulin if treating hyperglycemia to achieve a target glucose level of 180 mg/dL or less.

Post procurement care

76. Detection, registration and reporting of serious adverse events to the transplant center.
77. Debriefing by the donor coordinator and/or transplant coordinator about the results of the transplantation (anonymous) to the relatives, health care professionals and primary care physician.
78. Offering, if necessary, support to the relatives, for example by a feedback conversation after a couple of weeks or information about associations for relatives.

79. Debriefing with the involved health care professionals and transplant coordinator.
80. Ensuring the hospitalization invoice of the patient is excluded of any medical, pharmaceutical or hospital costs after the determination of brain death and legal declaration of death.

QUESTIONNAIRE PART III: QUALITY INDICATORS (DELPHI ROUND 2)

First round: please comment on the listed quality indicators if they are not well formulated for you or add new ones.

For example: quality indicator X
Comments on this quality indicator: .....
Reference(s): .....

Second & third round: please evaluate the listed set of quality indicators for the attributes relevance and feasibility on a 9-point Likert Scale, with 1 indicating "strongly disagree" and 9 "strongly agree".

- Relevance: the indicator truly measures the quality of care for the management of a donor after brain death in a perspective of organ donation (that is useful for professionals) [29].
- Feasibility: are data available and collectable, albeit contained within medical records or health authority datasets [29]?

For example: quality indicator X

	Strongly disagree				Undecided				Strongly agree
	1	2	3	4	5	6	7	8	9
Relevance	☐	☐	☐	☐	☐	☐	☐	☐	☐
Feasibility	☐	☐	☐	☐	☐	☐	☐	☐	☐

Definition of consensus after the third round

A quality indicator will be accepted with agreement if the attribute relevance has a median score of 7 or more with 75% of more of the ratings in the highest tertile (Likert score: 7-9) and the attribute feasibility has a median score of 7 or more.

Structure indicators

A measure that indicates the type and amount of resources used by an organization to deliver a key intervention.

1. Existence of donation process procedures.

   Formula: existence of procedures for all relevant steps of the donation process?

2. Existence of a proactive donor detection protocol.

   Formula: existence of a donor detection protocol?

3. Donation team (see glossary) full-time availability.

   Formula: availability of the donation team 24/7?

4. Documentation of key interventions of the donation process.

   Formula: existence of a documentation form with all relevant key interventions of the donation process?

5. Seminars on organ donation.

   Formula: number of organ donation seminars organized last year?

Process indicators

A measure that indicates the performance of (compliance with) a key intervention.

6. Detection of all potential donors after brain death in the ICU.

   Formula: number of potential donors after brain death in the ICU who are referred to the donor coordinator / number of potential donors after brain death in the ICU.

7. Evaluation of donors after brain death.

   Formula: number of patients declared brain death in the ICU who have been evaluated as donors in consult with a transplant center / number of patients declared brain death in the ICU.

8. Donor management goals.

   Formula: number of actual donors after brain death (see glossary) in the ICU meeting 5 of the 7 donor management goals prior to organ recovery (mean arterial pressure: 60-110 mm Hg, number of vasopressors ≤ 1, arterial blood gas pH: 7.3-7.5, serum sodium: 135-155 mEq/L, blood glucose: ≤ 180 mg/dL, urine output: ≥ 0.5 mL/kg/h over 4 hours, core body temperature: 35-37°C) / number of actual donors after brain death in the ICU.

9. Documentation of cause of no donation.

   Formula: number of failed potential donors in which the cause of no donation is properly documented / number of failed potential donors.

10. Documentation of evaluation of potential donors.

    Formula: number of donors correctly evaluated / number of donors evaluated.

Outcome indicators

A measure that indicates the result of a performance (or non-performance) of a key intervention.

11. Family objection to organ donation.

    Formula: number of objections (number of potential donor after brain death cases with family objection to organ donation) / number of families interviewed (number of potential donor after brain death cases in which family members are informed about the possibility of organ donation). *exclusion of donor cases where the patient's wishes are known (formal or informal).*

12. Conversion rate in donors after brain death.

    Formula: number of actual donors after brain death / number of eligible donors after brain death (see glossary).

Glossary

Potential donor after brain death: a person whose clinical condition is suspected to fulfill brain death criteria [30].

Eligible donor after brain death: a medically suitable person who has been declared death based on neurologic criteria as stipulated by the law of the relevant jurisdiction [30].

Actual donor after brain death:
A consented eligible donor [30]:

A. In whom an operative incision was made with the intent of organ recovery for the purpose of transplantation.

OR

B. From whom at least one organ was recovered for the purpose of transplantation.

Utilized donor after brain death: an actual donor from whom at least one organ was transplanted [30].

Donation team: the local donor coordination function should be performed by a multidisciplinary team (or donation team) consisting of at least one nurse and one specialist physician with a special professional title in intensive care (with 5 years' experience on an intensive care or emergency unit).

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