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A Systematic Review of Factors Influencing Decisions to Limit Treatment in the Emergency Department

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Contributor Statement

DJL and NW conceived and designed the study. NW acquired the data. NW, DJL, and IAS analysed and interpreted the data. NW drafted the manuscript and all authors contributed substantially to its revision. JES and PMT substantively reviewed and edited the manuscript. NW takes responsibility for the paper as a whole.

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Abstract

Background

Emergency physicians are frequently faced with making decisions regarding how aggressive to be in caring for critically ill patients. We aimed to identify factors that influence decisions to limit treatment in the Emergency Department through a systematic search of the available literature.

Design

Prospectively registered systematic review of studies employing any methodology to investigate factors influencing decisions to limit treatment in the Emergency Department. Medline and EMBASE were searched from their inception until January 2019. Methodological quality was assessed using the Mixed Methods Appraisal Tool, but no studies were excluded based on quality. Findings were summarised by narrative analysis.

Results

10 studies published between 1998 and 2016 were identified for inclusion in this review, including 7 cross-sectional studies investigating factors associated with treatment-limiting decisions, 2 surveys of physicians making treatment-limiting decisions and 1 qualitative study of physicians making treatment-limiting decisions. There was significant heterogeneity in patient groups, outcome measures, methodology, and quality. Only three studies received a methodology-specific rating of 'high quality'. Important limitations of the literature include the use of small single-centre retrospective cohorts often lacking a comparison group, and survey studies with low response rates employing closed-response questionnaires. Factors influencing treatment-limiting decisions were categorised into 'patient and disease factors' (age, chronic disease, functional limitation, patient and family wishes, comorbidity, quality of life, acute presenting disorder type, severity, and reversibility), 'hospital factors' (colleague opinion, resource availability), and 'non-patient healthcare factors' (moral, ethical, social, and cost factors).

Conclusions

Several factors influence decisions to limit treatment in the Emergency Department. Many factors are objective and quantifiable, but some are subjective and open to individual interpretation. This review highlights the complexity of the subject and the need for more robust research in this field.

Key words:

- Decisions to limit treatment
- Ceiling of treatment
- Systematic Review
- Emergency Department
- Decision Making

Key Messages:

What is already known on this subject:

- Optimisation of end-of-life care in emergency patients remains an area of uncertainty and has been identified as a research priority by clinicians, patients, and carers.
- Understanding the factors that influence decisions to limit treatment is a first step in designing decision-making aids and educational interventions to improve care delivery.

What this study adds:

- In this systematic review of 10 applicable studies on this topic, we found that decisions to limit treatment in the Emergency Department are influenced by patient and disease factors, hospital factors, and non-patient healthcare factors.
- Resource availability, cost factors, and cultural factors were also shown to influence decision making, highlighting potential ethical issues in a group of patients who are often unable to directly participate in the decision-making process.
- The variety of factors and influences suggest the need for a more standardized approach to decision making in these cases.

Introduction

Emergency Physicians (EPs) frequently face decisions concerning the institution of appropriate treatment for critically ill patients. [1] Developing a rational, consistent approach to these difficult decisions in the Emergency Department (ED) is becoming more important as developed countries face an ageing and increasingly multimorbid patient population. [2,3] Furthermore, the optimisation of end-of-life care in emergency patients has been highlighted as one of the top five research priorities in a recent UK research priority setting partnership involving clinicians, patients, and carers. [4]

This review focuses on decisions made when there is an advance recognition that certain interventions, settings or clinical contexts may not be appropriate in a clinical situation. In the UK, the phrase "Ceilings of Treatment" is in use, but this phrase is not is not widely used in an international context or conclusively defined in the literature, especially within the context of Emergency Medicine. [5] These crucial decisions to limit treatment should aim to maximise patient autonomy, enhance quality of life, improve patient and family experience of the care process, align with the wishes and beliefs of patients and family, and avoid the excessive allocation of limited resources to provide unwanted and futile life sustaining treatment. [6,7]

Treatment-limiting decisions can be challenging and complex in the ED. Patients may present across the continuum from the end of a long illness with well-defined expectations and an established advance care plan, or they may present with a devastating illness of sudden onset that is irreversible and requires palliation. Similar decisions are commonplace in palliative and other inpatient medical settings, but are usually made with reference to more detailed information. In the ED, decisions concerning patients who present with compromised physiology and multiple significant comorbidities often have to be made within narrow time-frames by physicians frequently lacking crucial information regarding patient wishes, medical history, pre-morbid state, a prior relationship with the patient's family, and where the patients frequently lack capacity to make important decisions about their own care. [1,8–10] The availability of advance care plans remains low in this environment. [1,11–13]

Additionally, physicians face a wider challenge in which the issue of death and dying requires patients and their families to confront deeply held societal norms. [14]

Effective and appropriate decision-making can improve patient and family experience of the dying process and reduce the burden of unnecessary hospital stay on patients and healthcare systems. [7,15] However, despite the benefits of early ED-based identification of patients appropriate for end-of-life care, there is significant uncertainty and variability in decision-making between physicians and units. [16–18] Recognising in advance the potential limits of any treatment is a part of this process, but many other factors may play into this decision.

Understanding factors associated with these decisions could inform the creation of decision-making aids and educational interventions designed to improve care delivery. The aim of this systematic review is to identify factors affecting decisions to limit treatment in the ED.

Methods

Protocol and Registration

Search criteria, inclusion and exclusion criteria, risk of bias assessment and data synthesis methods were specified in advance and documented in the International prospective register of systematic reviews (PROSPERO), registration number: CRD42018094751. [19] Patients or the public were not involved in the design, conduct, reporting, or dissemination plans of this review.

Search Strategy

A search of studies published in English in Medline and EMBASE from their inception until January 2019 was conducted using a structured strategy designed to answer the question 'what factors influence decisions to limit treatment by Emergency Physicians for patients presenting to the ED?'. Search terms were identified from key word lists of related publications and developed empirically by the authors, according to recommendations from the PRISMA and MOOSE guidelines of systematic

searches of observational studies. [20,21] *Appendices 1 and 2* outline the search algorithms employed. Reference lists of included studies were hand searched for additional papers.

Study Selection and definitions

Studies employing any methodology to explicitly investigate factors ED physicians stated influenced decisions to limit treatment, or reporting associations between patient or healthcare provider characteristics and treatment-limiting decisions were included. We considered any type of decision explicitly affecting the 'highest' level of intervention deemed appropriate by a medical team. Studies where the full text could not be obtained following reasonable attempts to contact the authors were excluded, as were papers not featuring original research. Full exclusion criteria were prospectively outlined on PROSPERO. [19]

Data extraction

Data were extracted separately by NW and IS, and checked by DJL. Extracted data included: author's name, date and country in which the study was performed, type of study, patient group and sample size, main aims and outcome measures. Variables or characteristics found to influence decision-making were recorded, with point estimates of association and measurements of statistical significance where applicable.

Statistical analysis

Heterogeneity in design, definition, and study populations precluded the use of meta-analytic techniques. Findings were instead tabulated and then summarised by detailed narrative analysis in accordance to the PRISMA checklist. [20]

Quality assessment

Each study included for data synthesis was quality assessed by NW and DJL separately using the Mixed Methods Appraisal Tool (MMAT). [22] Any discrepancies in quality assessment scores were discussed until a consensus was reached. MMAT is an effective and practical tool for the quality assessment of

quantitative, qualitative, or mixed methods studies within their methodological domain. It yields comparable quality ratings ranging from 0% (low quality) to 100% (high quality) based on four methodology-specific criteria. Its validity and reliability meet accepted standards and it has been pilot tested for reliability in systematic reviews. [23,24] Studies were not excluded from the review due to low quality scores - these were instead reported and discussed in the narrative synthesis.

Results

Search Results

Following the removal of duplicates, 5448 references were retained. 5404 papers were excluded on initial title and abstract screening based on prospectively outlined exclusion criteria. [19] The full texts of 44 eligible papers were read and reviewed by NW, IS and DJL. A further 35 studies were excluded. Disagreements between researchers were discussed until a consensus was reached. The reference lists of the nine full-text articles included were searched for additional eligible studies, and one additional study was identified for inclusion. Finally, ten papers were included for data extraction and qualitative synthesis. *Figure 1* outlines the study selection process.

Study Characteristics

Characteristics of included studies are summarised in *Table 1.* Seven cross-sectional studies, two survey studies, and one qualitative study were included. Settings included France, Belgium, Spain, Morocco, and Australia.

There was considerable heterogeneity in patient groups, outcome measures and methodology. Cross-sectional methodologies included either patients who died in the ED (5 studies), where there was a clear decisions to limit treatment (1 study), or elderly patients where patient and physician factors that were associated with a decision regarding limitation of treatment were identified (1 study). [1,8,25–29] Of the seven cross-sectional studies, all but two (both De Decker et al. studies) also included surveys or interviews (Rodriguez-Molinero et al.) of physicians investigating the factors that

physicians felt influenced decision-making in real time. [1,8,25,26,29] Two additional studies (Biegler et al. and Wong et al.) asked physicians to complete self-administered questionnaires featuring hypothetical scenarios. [30,31] Finally, one qualitative study (Fassier et al.) employed participant observation and physician interviews at the ED-ICU interface. [12]

Several studies were subject to important methodological limitations. Two of the cross-sectional studies (Le Conte et al. 2004 and De Decker et al. 2012) were small, single-centre studies lacking a comparison group, precluding attempts at multivariate regression. [8,30] Damghi et al. employed retrospective single-centre cross-sectional methodology susceptible to selection bias and confounding factors. [25] Among 5 cross-sectional studies that also included physician surveys, 4 used pre-specified criteria to determine the factors considered important by physicians, limiting the range of potential responses elicited, and how these were selected is mostly unclear. [1,8,25,26,29] Two survey-based papers (Biegler et al. and Wong et al.) and a cross-sectional study (Rodriguez-Molinero et al.) used hypothetical deteriorations of real patients or hypothetical scenarios to elicit decision-making. [26,30,31]. Five cross-sectional studies only recruited patients who died in the ED, potentially excluding a cohort of patients with treatment-limiting decisions who died elsewhere or survived to discharge without treatment escalation. [1,25,27–29] Finally, most cross-sectional studies only included patients for whom a treatment-limiting decision was made, resulting in the exclusion of patients where treatment-limitation was debated, but full escalation was felt to be appropriate. [1,8,25,27–29]

Study Quality

A structured assessment of quality contextualised by methodology using MMAT is reported in table 2. Of note, Biegler et al.'s survey exhibited limitations concerning sampling and response rate, whilst Wong et al.'s survey risked participation bias with a response rate of 13%. [30,31] Given the relatively small number of studies selected and the narrative synthesis of results, no studies were excluded.

Table 2: Quality rating using the Mixed Methods Appraisal Tool (MMAT). Asterisk denotes achievement of criteria.

		Studies									
Design	**Methodological Quality Criteria**	*Le Conte (a)*[8]	*Le Conte (b)*[1]	*Damghi*[25]	*Rodriguez-Molinero*[26]	*De Decker(a)*[28]	*De Decker (b)*[27]	*Richardson*[29]	*Biegler*[30]	*Wong*[31]	*Fassier*[12]
Quantitative non-randomised	Are Participants recruited in a way that minimizes selection bias?	*	*		*	*	*	*			
	Are measurements appropriate regarding the exposure/intervention and outcomes?	*	*	*	*	*	*	*			
	In the groups being compared, are the participants comparable, or do researchers take into account the difference between the groups?		*	*		*					
	Are there complete outcome data, and when applicable, and acceptable response rate, or an acceptable follow-up rate for cohort studies?	*	*	*	*	*	*	*			
Quantitative descriptive (survey)	Is the sampling strategy relevant to address the quantitative research question?									*	
	Is the sample representative of the population understudy?										
	Are measurements appropriate?								*	*	
	Is there an acceptable response rate?										
Qualitative	Are the sources of qualitative data relevant to address the research question?										*
	Is the process for analysing qualitative data relevant to address the research question?										*
	Is appropriate consideration given to how findings relate to the context in which the data were collected?										*
	Is appropriate consideration given to how findings relate to the researchers' influence?										*
		75%	*100%*	*75%*	*75%*	*100%*	*75%*	*75%*	*25%*	*50%*	*100%*
		Overall Quality Score									

Table 1: characteristics of included studies

Paper, country, year	**Type of Study**	**Patient group, sample size**	**Main Aim**	**Main outcome measure**
Le Conte et al., France, 2004[8]	Prospective, single centre, cross-sectional survey	All adult non-trauma patients for whom a decision to withhold (WH) or withdraw (WD) life sustaining treatment was made by senior ED staff between January 1998 and September 1998. n=119	Identifying clinical situations where life-support was withheld/withdrawn, and the criteria used by physicians to justify their decisions.	Characteristics of patients with treatment withhold/withdraw decisions. Pre-defined criteria used to justify treatment withhold/withdraw decisions.
Le Conte et al., France, 2010[1]	Prospective, multicentre, cross-sectional survey	All patients who died over two 2-month periods in 2004 and 2005 across 174 EDs in France (171) and Belgium (3). n=2420	Describing patients who died in the ED, studying the number of patients for whom a decision to limit life support was taken and describing the process leading to such decisions.	Association between patient characteristics and decision to withhold/withdraw life support therapies, using multivariate logistic regression analysis. Pre-defined criteria used to justify treatment withhold/withdraw decisions.
Damghi et al., Morocco, 2010[25]	Retrospective, single centre, cross-sectional survey	All patients who died in a Moroccan ED over a 5-month period in 2009. Patients with brain death or who died in transit to the ED were excluded. n=177	Assessing the frequency of situations where life-support therapies were withheld/withdrawn and modalities for implementation of these decisions.	Univariate analysis of patient characteristics significantly associated with treatment withhold/withdraw decisions. Multivariate logistic regression of patient characteristics associated with treatment withhold/withdraw decisions. Pre-defined criteria used to justify treatment withhold/withdraw decisions.

Rodriguez-Molinero et al., Spain, 2010[26]	Prospective, multicentre, cross-sectional study	Elderly patients (older than 80 years or 65-79 years with at least 2 comorbidities), their physicians and their relatives, across 4 EDs over 5 months in 2003 in Spain. Decisions based on patient/relative preferences, or on moral issues were excluded from multivariate analysis. n=101	Analysing the elements that compose the emergency physicians' criterion for selecting elderly patients for intensive care treatment.	Multivariate logistic regression of factors affecting treatment-limitation decisions regarding CPR/ICU/CCU Physician-reported criteria used to justify treatment withhold/withdraw decisions as advance directives.
De Decker et al., France, 2012[28]	Prospective, multi centre, cross-sectional study	All patients ≥65 years old who died over two 2-month periods in 2004 and 2005 across 174 EDs in France (171) and Belgium (3). n=2095	Determining whether the Charlson Comorbidity Index was associated with treatment-limiting decisions made for older patients who die in EDs.	Univariate analysis of patient characteristics associated with treatment-limiting decisions. Multivariate logistic regression of patient characteristics associated with treatment-limiting decisions.
De Decker et al., France, 2012[27]	Retrospective, single centre, cross-sectional study of patients who died in ED	All patients who died in one ED in France between April 2008 and September 2009 were retrospectively included. n=184	Determining whether the Kaplan Feinstein Index score was associated with treatment-limiting decisions in older adults dying in the ED.	Univariate analysis of patient characteristics associated with treatment-limiting decisions. Association between KFI score and treatment-limiting decisions on a multivariate logistic regression model.
Richardson et al., Australia, 2016[29]	Prospective, multicentre, cross-sectional questionnaire-based case series of deaths in the ED.	Every adult or child who died in 6 EDs in Australia with a decision to withdraw/withhold made solely by Emergency Physicians (EPs) or Emergency Registrars (ERs), n=320.	Describing differences between EPs and ERs in the importance placed on factors influencing withholding or withdrawing life-sustaining healthcare	Frequency of factors and discussions being reported as very important by EPs and ERs when making decisions to withhold or withdraw life-sustaining healthcare

Biegler et al., Australia, 1998[30]	Survey based on a hypothetical scenario.	All Emergency Physicians in Victoria, Australia. n=46 (67% of 69)	Determining which factors most influence Emergency Physicians' decisions to institute or withhold intubation for a hypothetical patient with life threatening illness. (closed responses)	Factors regarded as important in the initial decision on whether to intubate or not. Factors causing reversal of initial decision.
Wong et al., Australia, 2012[31]	Survey based on hypothetical scenarios.	Members of the Australian College for Emergency Medicine residing in Australia or New Zealand. n=388 (13% of 2992)	Identifying the decisions and attitudes of emergency clinicians in hypothetical scenarios involving advance directives. (closed responses)	Factors influencing decisions on commencing full treatment, limiting treatment, or palliation in three hypothetical scenarios involving advance directives.
Fassier et al., France, 2016[12]	Non-participant qualitative observational study supplemented by interviews.	Physicians observed making ED end-of-life decisions for elderly patients were identified and interviewed in 2010 in 2 hospitals in France. n=24 (15 ED and 9 ICU physicians)	Exploring physicians' perceptions and attitudes toward triage and end-of-life decisions for elderly critically ill patients at the ED-ICU interface.	Themes and axial codes identified as factors affecting end-of-life decisions.

Table 3: Cross sectional studies: Variables associated with decisions to limit treatment in the ED. S = statistically significant association. D = descriptive statistics used only. N = tested but no association identified. - = Not tested in this study.

		Le Conte (a)[8]	*Le Conte (b)*[1]	*Damghi*[25]	*Rodriguez-Molinero* [26]	*De Decker (a)*[28]	*De Decker (b)*[27]	*Richardson*[29]
Patient and disease factors	Age	D	S	S	S	S	N	-
	Chronic Disease	D	S*	S†	S‡	S‡N§	-	-
	Acute presenting disorder	D¶	S#	S**	-	S††	S§§	-
	Functional limitation	D	S	-	S	S	N	-
	Patient wishes	D	D	D	-	-	D	-
	Family wishes	D	D	D	-	-	D	-
	High illness severity	D	-	S	-	S	-	-
	Comorbidity	-	-	S	-	S	N	-
	Living in a long-term care facility	-	-	-	-	S	N	-
	Inpatient in previous year	-	-	-	-	S	N	-
Hospital factors	Discussion with nursing staff	D	D	D	-	-	-	-
	Discussion with other ED physicians	D	D	D	-	-	-	-
	Discussion with hospital specialist	-	D	-	-	-	-	-
	Discussion with GP	-	D	-	-	-	-	-
	Physician grade	-	-	-	-	-	-	S
	Long stay in the ED before death	-	-	-	-	-	D	-

** Chronic disease, chronic immunodeficiency, chronic liver disease*

† Chronic disease, chronic cardiovascular disease, chronic malignancy

‡ Chronic disease, chronic neuropsychiatric disease

§ Chronic cardiovascular disease, malignancy, chronic metabolic, chronic respiratory disease

¶ Acute neurological, respiratory, cardiovascular, gastrointestinal, cancer disorders

 # Acute neurological, respiratory, cardiovascular, brain haemorrhage, trauma disorders

*** Acute neurological disorders*

†† Acute neurological, respiratory, renal, haematologic disorders

§§ Acute neurological, respiratory, cardiovascular, infectious disorders

Table 4: Cross sectional and survey studies: physician-reported criteria influencing decisions to limit treatment in the ED. D = described by participants. N = tested but not described as influential. - = not tested in this study.

		Le Conte (a)[8]	*Le Conte (b)*[1]	*Damghi*[25]	*Rodriguez-Molinero*[26]	*Richardson* [29]	*Biegler*[30]	*Wong*[31]
Patient and disease factors	Age	D	D	D	D	D	D	-
	Underlying chronic disease	D	D	D	-	-	D	-
	Acute presenting disorder	D	D	N	D	-	-	-
	Irreversibility of acute disorder in first 24h	D	D	D	-	-	D	-
	Previous functional limitation	-	D	D	D	-	D	-
	Patient wishes	D	-	-	D	D	D	-
	Family wishes	D	-	-	D	D	D	-
	Comorbidities	-	-	-	D	D	-	D
	Underlying disease expected to be fatal within 6 months	D	D	N	-	-	-	-
	Level of care considered maximal	D	D	D	-	-	-	-
	Expected poor post-morbid quality of life	D	D	D	-	-	-	-
	Pre-morbid quality of life	-	-	-	D	-	D	-
	Absence of improvement following active treatment	-	D	D	-	-	-	-
	Prior mental status	-	-	-	D	-	-	D
	Presence of advance directive	-	-	-	-	D	-	D
	High severity of illness	D	-	-	-	-	-	-
	On home oxygen	-	-	-	-	-	D	-
	Nursing home resident	-	-	-	-	-	D	-
	Severe dementia	-	-	-	-	-	D	-
	Prognosis	-	-	-	-	D	-	-
	Physician perception of patient's interests	-	-	-	-	D	-	-
	Futility	-	-	-	-	D	-	-
Hospital factors	Discussion with ICU	-	-	-	-	D	-	-
	ICU bed availability	-	-	-	-	D	-	-
	Seniority of physician	-	-	-	-	-	-	D
Non-patient healthcare factors	High cost of care	-	-	D	-	-	-	-
	Moral considerations	-	-	-	D	-	-	-
	Ethical and professional responsibility	-	-	-	-	-	-	D
	Social status	-	-	-	D	-	-	-
	Organ donation	-	-	-	-	D	-	-

The studies identified in this review generally assessed two outcome measures: association of measured variables with treatment-limiting decisions (Table 3); in other words 'who are these decisions made for', and factors reported by Emergency Physicians as influencing these decisions (Table 4) - and 'how do we think we made these decisions?'. Factors can be loosely grouped into 'patient and disease factors', 'hospital factors', and 'non-patient healthcare factors'. Consistent findings are described below, including a summary of the statistical analyses undertaken. The purely qualitative study is described narratively.

Factors affecting decisions to limit treatment in cross sectional and survey studies:

Age

Five of the cross-sectional studies demonstrated an association between age and decisions to limit treatment. [1,8,25,26,28] In the most robust prospective multicentre cross-sectional study, Le Conte et al. (2010) found age to be independently associated with decisions to withhold or withdraw care in the ED through multivariate logistic regression analysis of 2420 patients who died in 174 EDs (71–81yrs OR=1.60 [95% CI: 1.18–2.16], 81–88yrs OR=2.51 [95%CI: 1.78–3.52], >88yrs OR=3.27 [95%CI: 2.26–4.71]). [1] Three other cross-sectional studies demonstrated statistical association between age and treatment-limiting decisions: De Decker et al. (age ≥85 years OR=20.33 [95% CI: 3.86-107.20]), Damghi et al. (OR = 1.1 [95% CI = 1.01-1.07]), Rodriguez-Molinero (OR 0.76 [95% CI: 0.59-0.97]). [25,26,28] A second study by De Decker et al. failed to demonstrate statistical association between age and decisions to limit treatment; however, this study included older adult patients only (mean age 86 $\pm$ 6). [27]

Age was self-reported as influencing 24% to 43% of decisions to limit treatment made by surveyed Emergency Physicians in six included studies. [1,8,25,26,29,30]

Chronic disease

Decisions to limit treatment were often associated with the presence of chronic disease. Le Conte et al. (2010) found that chronic immunodeficiency (OR= 1.90 [95% CI: 1.10-3.28]), liver disease (OR= 2.18 [95% CI: 1.43-3.31]) and metastatic cancer (OR= 2.34 [95% CI: 1.56-3.52]) influenced decisions to limit treatment. [1] Damghi et al. found association with underlying malignancy (OR = 3.4 [95% CI: 2.06-28.55]) and chronic heart failure (OR = 7.7 [95% CI: 1.38-8.54]). [25] De Decker et al. showed association between chronic diseases with functional impairment and treatment-limiting decisions on univariate analysis (p=0.009), but did not demonstrate significant association between these decisions and underlying malignancy or cardiovascular disease, in contrast with Damghi et al. [28]. Chronic respiratory disease appeared to be an independent factor inversely associated with treatment-limiting decisions in the De Decker study (OR= 0.17 [95% CI: 0.03-0.97]). [28]

Chronic debilitating disease was an important consideration by Emergency Physicians when making treatment-limiting decisions in 22% (Le Conte et al. 2010), 35% (Le Conte et al. 2004), 32% (Damghi et al.), and 61% (Biegler et al.) of cases. [1,8,25,30]

Acute presenting disorder

Decisions to limit treatment were commonly associated with acute neurological and respiratory presenting disorders. [1,8,25,27,28] Respiratory acute presenting disorders were found to be independently associated with decisions by Le Conte et al. (2010) (OR = 1.61 [95% CI: 1.21-2.13]), and De Decker et al. (OR = 7.89 [95% CI: 1.40-44.33]). [1,28] Acute neurological presenting disorders were found to be associated with decisions to limit treatment by Le Conte et al. (2010) (OR = 1.91 [95% CI = 1.39-2.62]), De Decker et al. (OR = 16.12 [95% CI = 2.70-96.07]), and Damghi et al. (OR = 4.1 [95% CI = 1.48-11.68]). [1,25,27] In contradiction to this, De Decker et al. found neurological causes of organ failure to be inversely associated with decisions to limit treatment (OR = 0.2 [95% CI = 0.06-0.68]. [28] Treatment-limiting decisions were associated with a number of other acute presenting disorders in individual studies, but less frequently tested overall (Table 3).

"Principal acute presenting medical disorder" was the most frequently cited factor affecting treatment escalation decisions in two studies that performed surveys of physicians, influencing 77% and 83% of decisions to withhold or withdraw treatment. "Underlying disease expected to be fatal within 6 months" also influenced 20% and 37% of decisions in the same studies. [1,8] In their survey of physicians, Rodriguez-Molinero et al. found that the presenting medical disorder influenced 18% of decisions regarding continuance of cardiopulmonary resuscitation or admission to intensive care units. [26] Of note, no physicians chose "acute presenting disorder" or "underlying disease expected to be fatal within 6 months" from a pre-defined list of factors influencing treatment limitation of 54 patients who died in ED in Damghi et al.'s survey. [25]

Functional limitation

Le Conte et al.'s (2004) cohort of patients for whom a treatment-limiting decision was made were severely functionally limited in 53% of cases. [8] Le Conte et al. (2010) showed that severe functional limitation was independently associated with decisions to withhold or withdraw treatment (Knauss C OR= 3.54 [95% CI: 2.66-4.70]), Knauss D OR= 5.84 [95% CI: 3.94-8.66]). [1] Rodriguez-Molinero et al. found functional limitation as assessed by physicians to be associated with decisions to limit treatment ($p<0.001$). [26] De Decker et al. showed significant association between functional limitation and decisions to limit treatment ($p<0.001$) in one study, but failed to show significant association in another, smaller study. [27,28]

Prior functional limitation was used by physicians in considering 38% (Le Conte et al. 2010), 69% (Rodriguez-Molinero et al.) and 6% (Damghi et al.) of treatment-limitation decisions. [1,25,26] Functional status was considered important in 85% of decisions to intubate (Biegler et al.). [30]

Patient and Family wishes

Four cross-sectional studies included in this review described patient and family involvement in decisions to withhold or withdraw treatment. [1,8,25,27] Le Conte et al. (2010) reported that of 2420

patients who died in 174 EDs, only 8% had capacity to participate in decision-making (of which 32% were ultimately involved). Family was involved in decision-making in 58% of cases. [1] Similarly, Damghi et al. showed patient and family involvement of 11% and 27%, De Decker et al. 13% and 37%, and Le Conte et al. (2004) of 27% and 72%. [1,25,28]

Patient wishes influenced 2%, 8%, 32%, and 63% of treatment-limiting decisions in studies by Rodriguez-Molinero et al, Le Conte et al (2004)., Richardson et al., and Biegler et al. respectively. [8,26,29,30] Wong et al. found that the introduction of an Advance Directive expressing treatment-limiting wishes to hypothetical scenarios significantly impacted decisions to limit treatment. [31] 59% of physicians in Richardson et al.'s survey reported Advance Directives influencing decision-making. [29] Family wishes were cited by Emergency Physicians as influencing 2%, 56%, and 90% of decisions in Rodriguez-Molinero et al., Biegler et al., and Richardson et al.'s studies, respectively. [26,29,30]

High illness severity and Reversibility

Decisions to limit treatment were frequently statistically associated with high illness severity. Damghi et al. showed association between higher APACHE II scores and decisions to limit treatment ($p<0.001$), whilst De Decker et al. demonstrated association with 2 or more organ failures ($p<0.001$). [25,28] Perceived irreversibility of the acute presenting disorder was cited by Emergency Physicians as contributing factors in 54% (Le Conte et al. 2010), 60% (Le Conte et al. 2004), and 43% (Damghi et al.) of cases involving decisions to withhold or withdraw treatment. [1,8,25] Reversibility of illness was considered important in 98% of initial decisions to intubate (Biegler et al). [30] Physicians cited 'absence of improvement following a period of active treatment' as influencing 26% and 61% of decisions to limit treatment in Le Conte et al. (2010) and Damghi et al.'s studies respectively. [1,25] High illness severity was reported as influential in 40% of decisions to limit treatment in Le Conte et al. (2004). [8]

Comorbidities

Damghi et al. found that patients with treatment-limiting decisions had a higher Charlson Comorbidity Index ($p<0.001$), and a Charlson Comorbidity Index score of 5 or more was independently associated with treatment-limiting decisions (OR=25.56 [95% CI: 1.22-537.29] in one study by De Decker et al. [25,28]. De Decker et al. did not show significant association between severity of comorbidities (as measured by the Kaplan Feinstein Index) with treatment-limiting decisions in a smaller single-centre study. [27] Comorbidity was reported by physicians as influencing 30%, 37%, and 88% of decisions to limit treatment in Rodriguez-Molinero et al., Wong et al., and Richardson et al.'s studies, respectively. [26,29,31]

Discussion with ED physicians and nursing staff

Several studies reported involvement of ED physician and nursing colleagues in decision-making. Le Conte et al (2004) found that decisions to withhold or withdraw treatment were discussed with other medical and nursing staff in 39% and 31% of cases respectively. [8] In Le Conte et al.'s 2010 paper, decisions were made by at least 2 ED physicians in 80% of cases, with nursing staff involvement in 27%.[1] Damghi et al. found additional ED physicians involved in decision-making for 57% of cases and nursing staff involved in 89% of decisions. [25]

Quality of life

Poor predicted post-morbid quality of life was frequently cited in surveys of physicians. Le Conte et al. found that 39% and 25% of physicians considered this to be important in their 2004 and 2010 papers respectively. [1,8] Damghi et al. found that 33% considered quality of life to be influential. [25] 4% of physicians in Rodriguez-Molinero et al.'s paper cited pre-morbid quality of life as an important factor when making plans for treatment or therapeutic abstention concerning cardiopulmonary resuscitation or admission to intensive care units. [26] 83% of Biegler et al.'s respondents considered pre-morbid quality of life important when making decisions to intubate. [30]

Current level of care maximal

Three studies also found that 'current level of care considered maximal', described as "when more aggressive therapy would be unreasonable", was used to justify 17% (Le Conte et al. 2010), 59% (Le Conte et al. 2004) and 6% (Damghi et al.) of decisions to withhold or withdraw treatment. [1,8,25]

Factors affecting treatment escalation decisions in qualitative studies:

In Fassier et al.'s ED-based qualitative study of decisions to limit treatment using non-participant observations and semi-structured interviews, a major theme was 'physician's representation of the elderly'. Physicians conceptualised 'elderly' through the lens of old-age thresholds (younger than 70 years, 70-85 years, and over 85-years), physiological age as being either preserved or altered, and elderly stereotypes such as 'the independent super-grandpa' or 'the senile nursing home resident with dementia'. Personal familial experience of ageing also was identified as influential. Decisions were influenced by family member's wishes and were perceived as more straightforward when information about the patient's end-of-life preferences was available. Younger physicians with no training in end-of-life decision-making perceived treatment-limiting decisions to be complex, describing a psychological burden associated with doubt, uncertainty, guilt, and regret over making 'life or death decisions.' Experience and training in ICU and palliative care was perceived as making decisions easier. Decisions to limit treatment were perceived as complex, time intensive, and complicated by nightshifts, weekends, and handovers. Lack of time and lack of a dedicated 'relatives room' made decisions more challenging in the ED. [12]

Discussion

Main findings

Factors shown to influence decisions to limit treatment with consistency were broadly categorised into patient factors (age, chronic disease, functional limitation, comorbidity, quality of life), acute disease factors (type , severity, and reversibility of acute presenting disorder), and patient and family wishes. This was often in the context of discussion with medical and nursing

colleagues. There were several additional factors statistically associated with treatment-limiting decisions or considered important by physicians that were only reported in some papers, perhaps playing a more peripheral and context-dependent role in decision-making.

The association of measured variables with treatment-limiting decisions and factors reported by Emergency Physicians as influencing these decisions were largely congruent across different studies. However, there were some discrepancies between statistically associated factors and those reported important by physicians. These may be due to recall and reporting bias, or may suggest that clinicians' intentions do not always match their actions in practice, and that their actions may be influenced by external factors such as family wishes, legal considerations, societal norms.

The included studies represented a variety of social, cultural and economic situations, all of which may have influenced the individual study findings. While many of the findings of individual studies may have been generalisable to other healthcare settings, questions regarding the impact of healthcare system, resource availability, and cultural factors remain. For example, the study conducted by Damghi et al. in Morocco (the only middle-income country included in this review) uniquely found 'high cost of care' to be a factor used by physicians to justify 15% of treatment withhold/withdraw decisions. Financial barriers have previously been described in foregoing or delaying access to emergency care services in low, middle and high-income countries. [32]

Implications

Some identified factors raise ethical questions regarding the influence of cultural norms and the healthcare models within which these decisions are made on the decision-making process. For example the finding that resource factors (high cost of care, ICU bed availability) and subjective factors open to inherent bias (moral considerations, patient's interests, perceived quality of life and functional status) may play a role in decision-making invites questions on the ethics of considering these influences, and may help to explain the previously observed inter-physician variability. [16–18] The factor 'poor predicted post-morbid quality of life' is open to significant subjectivity and bias.

Furthermore, it assumes physicians can accurately predict outcome in critically ill patients. Physicians must be cognisant of the potential for bias when making decisions to limit treatment. This highlights the importance of a team approach to decision-making, and is perhaps an area in which clinical decision support can be beneficial.

Furthermore, a large proportion of the patient cohort included in this review lacked capacity to participate in the decision-making process, highlighting the importance of advance care plans and scope for initiatives such as the 'Recommended Summary Plan for Emergency Care and Treatment (ReSPECT)' to enhance patient autonomy and improve the quality of decision-making in the ED setting. [33]

This review highlights the complexity and need for more robust research to increase and validate our knowledge regarding the multitude of additional, less prevalent factors influencing treatment escalation decisions. Whilst commendable effort has been made to conduct high-quality, multi-centre observational studies with prospective design and innovative data collection methodology in this challenging field, limitations such as the use of surveys featuring pre-defined criteria may limit the scope of factors elicited. Our findings highlight that qualitative research may have a significant role to play in elucidating factors which may be unpicked with difficulty through observational and survey-based methodology alone.

Limitations

This review had several limitations. Firstly, language bias may have been introduced as the search was restricted to studies available in English. There is also potential for bias arising from study setting as only one study was conducted in a middle-income country (Morocco). Of the other nine studies included, five were conducted in France (one partially conducted in Belgium), three in Australia, and one in Spain. This may reflect that end-of-life care in general is not a research priority in low to middle income countries at this time.

GRADE-CERQual (Confidence in the Evidence from Reviews of Qualitative Research) methodology was employed to assess confidence in the findings of this review (Appendix 1 and 2). [34] This evaluation was however severely limited as it is based on a single qualitative study. Due to the relatively small number of manuscripts identified for inclusion, methodological limitations identified through MMAT assessment, and heterogeneous methodology employed by the included studies, the level of confidence in the conclusions made by this review is low. This emphasises the importance of further research in this important topic.

The review of this complex area of clinical practice benefited from a lack of methodology-specific exclusion criteria, resulting in the inclusion of several diverse study designs. However, this heterogeneity limited the ability for direct comparisons between studies or pooling of data in any meaningful manner. Furthermore, the variability of variables extracted for analysis and pre-defined factors measured makes discerning relative frequency and comparing findings difficult. As a result, this review was unable to quantitatively analyse the results of included studies using a meta-analytic approach, instead employing narrative synthesis. Lastly, this review did not seek to synthesise results based on weightings of quality. This may become a consideration as further work emerges.

Conclusion

This review highlights several factors affecting decisions to limit treatment. Some are objective and quantifiable, but others are subjective and open to individual interpretation. This raises potential ethical issues in the context of low patient and family participation in decision making.

Practitioners should be aware of this subjectivity and their biases when asked to make these decisions. In light of these findings, it would be prudent of Emergency Physicians to involve the wider clinical team in decision-making, while striving to include patients and their families wherever possible and appropriate.

This review highlights the need for larger scale, methodologically robust studies on the factors influencing treatment escalation decisions in Emergency Medicine, particularly as the ageing of the population inevitably will make these kinds of decisions more commonplace in the ED.

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