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Treatment limitations in intensive care units

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ABSTRACT

INTRODUCTION: Patients in intensive care units (ICUs) have treatment limited or withdrawn if further treatment is considered futile. This multicentre prospective observational study was part of a European study of patterns of limitations.

METHODS: In the first six months of 2016, all patients admitted to three Danish ICUs were screened and those with treatment limitations or death in the ICU were included. End-of-life outcomes were classified into five mutually exclusive categories: withholding, withdrawing, shortening of dying process, failed cardio-pulmonary resuscitation and brain death. This sub-study compared interdepartmental variation in limitation patterns among Danish ICUs.

RESULTS: A total of 1,132 ICU patients were admitted, and 264 (23.3%) had limitations to their treatment and/or died and were therefore included. Mortality among these patients was 71.5%, with interdepartmental differences of 52-85% in mortality, but no difference in overall mortality. Specifically, eight different limitations were described with distinct differences amongst departments, most likely due to case mix differences. A total of 96% of patients with limitations suffered from one or more chronic conditions, and 15-48% of the patients with limitations survived to ICU discharge.

CONCLUSION: Many Danish ICU patients have limitations imposed on therapy during their ICU stay, but large interdepartmental differences are primarily based on case mix differences. Although a large proportion of patients with limitations ultimately die, limitations do not portend imminent death.

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Even though admittance to an intensive care unit (ICU) may be immediately lifesaving and patients can be kept alive despite severe disease, their one-year mortality remains high. Therefore, treatment should be started and continued only as long as there is an expectation that the patient's situation will improve, and the patient should not be exposed to disproportionate treatment 1, 2. Consequently, a crucial part of the intensivist's job is to establish the clinical situation of each patient, determine if any chronic disease has an impact on the present situation, if possible, elucidate the treatment goals and the patient's wishes, make relevant treatment limitations if indicated and withhold or withdraw treatment if no hope for cure or benefit exists.

Based on data from 2000 and 2010, treatment limitations and ethical decision-making in Danish ICUs were

described from three and two Danish departments 3, 4.

From 1999 to 2016, a significant increase in limitations of life-prolonging therapies was found in 22 European ICUs; concomitantly, death without limitations in life-prolonging therapies decreased significantly 5. These findings suggest a shift in end-of-life (EOL) practices in European ICUs 5. In 2016, 2.1% of all admissions to Danish hospitals required ICU care, and data from the Danish Intensive Care Database indicate that the number of ICU admissions per capita decreased from 2007 to 2016 6. In view of these differences, the purpose of this multicentre study was to investigate EOL practices and decision-making processes in Danish ICUs and to investigate possible interdepartmental differences among Danish ICUs, which has not been done previously. As these data were part of a large European study, we also compared some of the Danish results with findings from European ICU studies.

METHODS

This study was part of a European prospective observational study 5. Consecutive patients admitted to three Danish ICUs during a self-selected, continuous six-month period from September 2015 to October 2016 were studied prospectively. Included were all ICU patients who died or had a limitation of life-sustaining interventions. Definitions of EOL practices were the same as in the Ethicus-1 study 3 and included withholding or withdrawing life-sustaining treatments, active shortening of the dying process, failed cardiopulmonary resuscitation (CPR) and brain death. A hierarchical categorisation was used if more than one active limitation occurred (active shortening of the dying process > withdrawing > withholding) 7. Follow-up continued until discharge from hospital, death in hospital or two months from the first limitation decision. Three Danish hospitals participated in the study: sites A, B and C. Data were presented as numbers/percentages with total numbers and numbers for the three participating sites. Interdepartmental differences in mortality and differences in the number of patients involved in decision-making compared with a former study were calculated using the chi-squared test.

All three participating hospitals had one ICU only at the time of the study. One ICU was part of a primary acute care hospital with trauma, medical and surgical patients; one was located in a hospital primarily serving medical patients and the third was both a general and a highly specialised ICU.

Permission to register data in a non-Danish database was granted by the Danish Data Protection Agency (2015-41-4474). Permission to access patient data without patient consent was granted by the Danish Patient Safety Authority (3-3013-1158/1/KWH).

Trial registration: not relevant.

RESULTS

In total, 1,132 patients were admitted to one of the three ICUs in the first six months of 2016, and 264 (23.3%) of these patients met the inclusion criteria. The patients' median age was 70.7 years (range: 18-94 years) and 148 (56%) were men. Among the ICU patients admitted at site A, 76 of 403 (18.8%) met the inclusion criteria; at site B, 86 of 460 (18.7%), and at site C, 102 of 269 (37.9%).

Interdepartmental differences were recorded in the distribution of limitations. Overall, withholding was seen in 11.2% of patients ranging from 6.1% to 20.4% in the three hospitals. Withdrawing was done among 10.5% of all patients, with a range of 6.5% to 17.5% at the three sites (**Table 1**).

TABLE 1 Distribution and types of limitations in the three hospitals as a percentage of admitted patients in each intensive care unit. The values are n (%).

	Hospital			
	Site A (N_A = 403)	Site B (N_B = 460)	Site C (N_C = 269)	Total (N_{tot} = 1,132)
Withheld	44 (10.9)	28 (6.1)	55 (20.4)	127 (11.2)
Withdrawn	26 (6.5)	46 (10.1)	47 (17.5)	119 (10.5)
Shortened dying process	0	1 (0.2)	0	1 (0.1)
Failed CPR[a]	4 (1.0)	7 (1.5)	0	11 (1.0)
Brain dead	2 (0.5)	4 (0.9)	0	6 (0.5)

CPR = Cardiopulmonary resuscitation.
a) Unsuccessful attempt to resuscitate in patients with no limitation set.

The types of limitations are shown in **Table 2**. The three most common limitations were: "Do not resuscitate" (DNR) found in 97.1%, 96% and 100% of all patients with limitations at sites A, B and C, respectively; followed by withholding of the endotracheal tube overall 56.3%, with interdepartmental differences ranging from 29.3% to 73.5%; and finally withdrawing of vasopressors, ranging from 22% to 49%. Table 2 also shows that eight different limitations were in effect.

TABLE 2 Therapies withheld or withdrawn. The values are n (%).

	Hospital			
	Site A (N_A = 70)	Site B (N_B = 75)	Site C (N_C = 102)	Total (N_{tot} = 247)
Do not resuscitate				
Withholding	68 (97.1)	72 (96.0)	102 (100)	242 (98.0)
Withdrawing	0	0	0	0
Endotracheal tube				
Withholding	42 (60.0)	22 (29.3)	75 (73.5)	139 (56.3)
Withdrawing	4 (5.7)	5 (6.7)	15 (14.7)	24 (9.7)
Mechanical ventilation				
Withholding	14 (20.0)	16 (21.3)	12 (11.8)	42 (17.0)
Withdrawing	14 (20.0)	13 (17.3)	37 (36.2)	64 (25.9)
Vasopressors				
Withholding	9 (12.9)	4 (5.3)	28 (27.5)	41 (16.6)
Withdrawing	18 (25.7)	37 (49.3)	23 (22.5)	78 (31.6)
Total parenteral nutrition				
Withholding	1 (1.4)	0	1 (1.0)	2 (0.8)
Withdrawing	2 (2.9)	3 (4.0)	3 (2.9)	8 (3.2)
Enteral feeding				
Withholding	5 (7.1)	0	0	5 (2.0)
Withdrawing	2 (2.9)	20 (26.7)	4 (3.9)	26 (10.5)
Intravenous fluids				
Withholding	0	0	0	0
Withdrawing	2 (2.9)	27 (36.0)	9 (8.8)	38 (15.4)
Haemodialysis				
Withholding	8 (11.4)	8 (10.7)	40 (39.2)	56 (22.7)
Withdrawing	2 (2.9)	16 (21.3)	12 (11.8)	30 (12.1)

The reasons for the limitations are shown in **Table 3.** The major reason and difference were “chronic disease” at 39% (range: 17-69%). Other reasons included: “no response to maximal therapy” at 17% (range: 8-29%) and neurological disorder at 15% (range: 6-21%). Limitations were discussed with 14.9% of the patients in the ICUs, with no obvious interdepartmental differences as the range was 14.3% to 16%, but this is significantly more than in 1999 when limitations were discussed only with 6.7% of the patients (p = 0.002). An advanced directive was present in 1.32%, 2.33% and 1.96% at sites A, B and C, respectively.

TABLE 3 Primary reason for limitation. The values are n (%).

	Hospital			
	Site A (N_A = 70)	Site B (N_B = 75)	Site C (N_C = 102)	Total (N_{tot} = 247)
Chronic disease	12 (17.1)	15 (20.0)	70 (68.6)	97 (39.3)
No response to maximal therapy	13 (18.6)	22 (29.3)	8 (7.8)	43 (17.4)
Neurologic disorder	15 (21.4)	17 (22.7)	6 (5.9)	38 (15.4)
Patient desire	10 (14.3)	12 (16.0)	15 (14.7)	37 (15.0)
Multi-organ failure	4 (5.7)	4 (5.3)	2 (2.0)	10 (4.1)
Family desire	6 (8.6)	1 (1.3)	0	7 (2.8)
Other reasons[a]	10 (14.3)	4 (5.3)	1 (1.0)	15 (6.1)

a) E.g. sepsis, poor quality of life, age.

Table 4 shows the main acute diagnoses among the admitted patients with limitations; the two primary diagnoses were respiratory and cardiovascular disease. The table also shows the most common primary and secondary chronic diseases among patients with limitations, with 96% of all included patients suffering from a chronic disease before admittance.

TABLE 4 Main acute diagnosis and chronic diseases for patients with limitations. The values are n (%).

	Hospital			
	Site A	Site B	Site C	Total
Main acute diagnosis				
Respiratory	28 (37)	28 (33)	60 (59)	116 (44)
Cardiovascular	14 (18)	49 (57)	4 (4)	67 (25)
Sepsis	8 (11)	2 (2)	17 (17)	27 (10)
Surgery	10 (13)	4 (5)	6 (6)	20 (8)
Other	12 (15)	1 (1)	6 (6)	19 (7)
Neurological	4 (5)	2 (2)	9 (9)	15 (6)
Subtotal	76	86	102	264
Main chronic disease				
Cardiovascular	21 (28)	42 (49)	55 (54)	118 (45)
Chest diseases	18 (24)	12 (14)	20 (20)	50 (19)
Neurological	12 (16)	6 (7)	10 (10)	28 (11)
General history	13 (17)	3 (3)	5 (5)	21 (8)
Other	7 (9)	9 (10)	3 (3)	19 (7)
Cancer	4 (5)	5 (6)	8 (8)	17 (6)
None	1 (1)	9 (10)	1 (1)	11 (4)
Subtotal	76	86	102	264
2nd chronic disease				
Cardiovascular	24 (44)	31 (54)	32 (38)	87 (44)
Chest diseases	5 (9)	4 (7)	15 (18)	24 (12)
Neurological	5 (9)	6 (11)	9 (11)	20 (10)
General history	14 (25)	10 (18)	11 (13)	35 (18)
Other	7 (13)	5 (9)	6 (7)	18 (9)
Cancer	0	1 (2)	11 (13)	12 (6)
Subtotal	55	57	84	196

Mortality varied among the included patients: 82.9% at site A, 84.9% at B and 52% at C ($p < 0.001$), whereas overall mortality at the three sites ranged from 15.6% at site A, to 15.9% at B and 19.7% at site C. The difference between the sites was not significant ($p = 0.31$). Only 1% of all patients died after failed CPR.

Among the Danish patients, 23% had limitations during their stay in the ICU versus 13% in the total sample of European admissions from the same database. Despite that, Danish ICU mortality was lower than in the rest of Europe: 72% versus 82% among patients with limitations 5.

DISCUSSION

Almost a quarter of the patients admitted to the three Danish ICUs had limitations on treatments, though with

interdepartmental differences. The Danish ICUs differ from their European counterparts by more frequently withholding and withdrawing treatments, but the difference has narrowed compared with comparable data in 1999 3. One possible explanation for these differences between Danish and European ICUs may be different triage patterns. Denmark has one of the lowest numbers of ICU beds per 1,000 inhabitants in Europe 8. Consequently, only very sick patients are admitted to Danish ICUs, possibly in a state of health where limitations are appropriate. Also, contrary to some European countries, legislation in Denmark allows for limitations without the consent of patient or relatives, provided limitations are based on documented clinical judgment and respect patient autonomy and that patients and relatives are informed about the decisions made 9.

In line with two previous Danish papers 3, 4, the most common withholding limitation was DNR with little variation among the three Danish ICUs. DNR was also the most frequent limitation in the rest of Europe 5. However, in total rather large interdepartmental differences were observed: 14% for withholding - and 11% for withdrawing. These differences are probably explained by variations in the case mix of admitted patients at the three sites. Site A, for instance, had the second highest number of cases in which endotracheal tubes were withheld (Table 2). This is in line with the fact that their most common acute diagnosis was respiratory disease (Table 4). Site B had the highest number of inotrope withdrawals; again, this in line with the fact that this is the only ICU with cardiothoracic surgery and hence many patients with cardiac disease. Site C had the highest number of limitations (Table 1) and concomitantly states chronic disease (where we know that long-term outcome is often worse) as the primary reason for limitations among 68% of its patients (Table 4). Chronic disease as the primary reason for limitation was stated only in 17% at site A and 20% at site B.

Such interdepartmental differences among Danish ICUs have not been described before but have been observed elsewhere. Thus, a systematic review from 2015 found a variation in the prevalence of withdrawal of life-sustaining treatment between world regions, between countries, between individual ICUs within culturally homogenous regions or countries, and, in one study, even between individual intensivists in a single ICU 10. Moreover, specific cultural, geographic, religious, statutory or physician-related factors may help explain the variability seen in withdrawal of life-sustaining treatment 10.

Individual intensivists do not always follow recommendations from international consensus statements 11, 12. An extreme example of departmental differences is a UK sample of 127 ICUs, where withdrawing ranged from 1.7% to 96.1%, with a nearly uniform distribution across those two extremes. However, here the substantial between-unit variability remained after accounting for case mix differences in admissions 13.

The number of limitations observed in this study may seem high, but in 40% of the included patients the primary reason for one or more limitations was that they suffered from chronic disease, corresponding to 96% of the included patients suffering from one or more chronic diseases, which will normally diminish their chances of survival. As noted before, the case mix at sites A and C showed many patients with chronic obstructive pulmonary disease, for which non-invasive ventilation in the ICU is an effective treatment, but the need for intubation is a poor prognostic sign which is therefore not necessarily offered or is declined by the patients. These ICU patients may be too ill to be cared for in a general ward, but the physicians and often also the patient do not necessarily equate ICU admission with full ICU treatment. They might, in fact, have been cared for just as well in an intermediary ward thus not counting as ICU patients.

We found a notable increase in patients who participated in decisions on limitations in the ICU, from 7% in the first Danish Ethicus study 3 to 15% in the present study. There may be several explanations for this finding. First, new Danish legislation demands greater respect for patients' autonomy 9. Second, the use of less analgesia and sedation for patients on non-invasive ventilation and patients on a ventilator makes it possible for patients to participate in decision-making 14; and, finally, it is our impression that Danish patients and relatives to a greater extent now than in 1999 do not want disproportionate ICU therapy. In 2.8% of the cases, family desire was the

primary reason for the limitation, but this was always supported by the clinical situation. Even though there were many differences among the three ICUs with respect to patient involvement, the three ICUs apparently work within the same ethical framework. Furthermore, at the time of the study, only two sites (A and C) had EOL guidelines, with no major differences in these guidelines.

Likewise, mortality among patients included in the study was different at the three sites, but among all admitted patients in the three sites, mortality was the same.

Comparing Denmark with Europe reveals a higher number of limitations in Denmark, but even so, Danish ICU mortality for patients with limitations was lower than in the rest of Europe 5. The Ethicus-2 study found a European mortality reduction from 12.2% to 10.7%, despite an increase in limitations compared with the 1999 Ethicus-1 study 5. One simple explanation for this may be that European and Danish doctors are more competent now, yielding higher survival rates. Another possible explanation has been provided by an Italian study. In 84 ICUs, 3,793 patients were followed for 12 months: ICUs with a high frequency of limitations had higher survival rates than ICUs with fewer limitations 15. The authors noted that, when one concentrates on patients who are likely to survive (rather than trying to save everyone), one achieves better overall results 15. Between 15% and 48% of the patients with limitations in the three Danish ICUs were discharged alive from the ICUs despite limitations, indicating that a limitation does not equal a decrease in survival rate but is merely an indication that the ICU staff consider some treatment possibilities inappropriate in a particular clinical situation.

The strengths of this study comprise the prospective reporting of actual bedside practice, and the participation of three of the five Danish regions including data from both university and regional hospitals. Thus, the results are hopefully representative for Danish ICUs. However, a risk of selection bias exists, as the three participating hospitals were not randomly selected but had previously participated in similar studies. Additionally, although 1,132 patients were screened for the study, they represented only about 4% of total ICU admissions to Danish hospitals in the study period.

CONCLUSIONS

Many patients in Danish ICUs have limitations imposed on life-sustaining therapy during their ICU stay. Their number of patients with limitations is proportionally higher in Denmark than in other parts of Europe. However, these limitations do not lead to a higher mortality level, and limitations do not portend imminent death. There are significant interdepartmental differences in both total numbers and types of limitations in Danish ICUs based on case mix. An increasing number of ICU patients are involved in the decisions concerning their treatment.

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