Avoidable 30-day mortality analysis and failure to rescue in dysvascular lower extremity amputees

Implications for future treatment protocols

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Background and purpose — An enhanced treatment program may decrease 30-day mortality below 20% after lower extremity amputations (LEA). The potential and limitations for further reduction are unknown. We analyzed postoperative causes of 30-day mortality, and assessed failure to rescue (FTR) rate in LEA patients who followed an enhanced treatment program.

Patients and methods — Medical charts of 195 primary LEA procedures were reviewed independently by 3 of the authors, and deaths during hospitalization following amputation were classified according to consensus.

Results — 31 patients died within 30 days after surgery. 4 deaths were classified as "definitely unavoidable," 4 as "probably unavoidable," and 23 as "FTR." Patients who died had a higher incidence of sepsis, pneumonia, and acute myocardial infarction compared with those alive. A log binominal regression analysis adjusted for age, sex, ASA score, diabetes, nursing home admission, transfemoral amputation (TFA), and BMI showed that the risk of 30-day mortality was increased for TFA (RR = 2.3, 95% CI 1.1–4.8) and for patients with diabetes (RR = 2.7, 95% CI 1.3–5.6). The FTR rate (patients with 30-day mortality/all patients with a severe postoperative complication) was 30%. Of the FTR deaths, 20 at some point had active lifesaving care curtailed.

Interpretation — Future initiatives should be directed at enhanced sepsis and pneumonia prophylactic actions, in addition to close monitoring of hemodynamics in anemic patients, with the potential to further reduce morbidity and mortality rates.

30-day mortality rates in excess of 30% have been reported in patients following a major dysvascular lower extremity amputation (LEA) (Kristensen et al. 2012). Beyond atherosclerosis or diabetes, treatment is most often challenged by several competing co-morbidities and high age (Kristensen et al. 2012, Wied et al. 2016). Perioperative optimization may reduce morbidity and mortality. Thus a recent study reported decreased mortality rates following an enhanced in-hospital treatment program (Kristensen et al. 2016), but the potential and limitations of a further reduction in mortality are unknown. The mortality rates are frequently used to compare the quality of treatment between hospitals. However, this has recently been challenged since some deaths in hospital are inevitable. As stated by Silber et al. (1992, 2007), the mortality is related to the degree of illness and co-morbidity of patients receiving treatment and not necessarily the expression of differences in the quality of care. Failure to rescue (FTR)—the probability of death if experiencing a severe postoperative complication—is becoming increasingly popular as an indicator showing how well hospitals perform once the complications occur (Silber et al. 1992, 2007).

The aim of this study is to analyze causes of 30-day mortality after LEA procedures and the FTR rate. We hypothesize that some of the 30-day deaths could be classified as FTR cases.

Patients and methods

Hvidovre University Hospital Copenhagen has a catchment area of around 600,000 people, and performs all non-traumatic amputations in the area resulting in approximately 100 major dysvascular LEAs per year. The study is a single-center

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retrospective cohort study of patients with a primary LEA admitted between January 2013 and April 2015. All patients with primary LEA were assessed for inclusion if the limb was amputated because of arteriosclerosis or diabetic complications. Exclusion criteria were bilateral amputation procedures and re-amputations.

All LEA patients follow a well-defined enhanced rehabilitation program, in an acute orthopedic ward (Kristensen et al. 2016).

Preoperative management

Patients referred from general practitioners, outpatient clinics, or emergency departments have their ankle-brachial blood pressure index measured, and their medical record is submitted to the vascular surgeons for the possibility for revascularization. If revascularization is deemed unobtainable by the Department of Vascular Surgery a supplementary measurement of skin perfusion pressure is performed to aid the decision on the amputation level. Senior consultants then review the indication for amputation. The patients are treated upon arrival at our department according to standardized fluid and transfusion protocols. The patients receive prophylactic antibiotics (dicloxacillin intravenously) before surgery and low-dose low-molecular-weight heparin after surgery.

Intraoperative management

The surgery is performed by trained residents or senior consultants. All transtibial amputations (TTA) procedures are performed approximately 12 cm below the knee joint, with sagittal flaps ad modum Persson (Persson 1974). The transfemoral amputation (TFA) procedure is performed with standard anterior and posterior skin flaps approximately 10 cm above the knee joint. Through-knee exarticulation (TKE) is rarely performed. The tissue vitality is assessed regularly during the operation, and the patient is informed of the risk of amputation at a more proximal level if tissue intraoperatively is deemed not to be vital. Spinal or general anesthesia is used during surgery. An ischiatic catheter with a continued infusion of (2 mg/mL) ropivacaine at a rate of (4 mL/h) with a possible bolus of 5 mL and 30 min lockout time is placed during the TFA. A peripheral nerve catheter with continuous infusion is applied after surgery for TTA to provide extended analgesia for the first 4 postoperative days.

Postoperative management

Postoperatively the oral intake of fluids is supplemented with 1.000 mL standard rehydration fluid (isotonic Na-K-glucose or Ringer's lactate) administered intravenously. Fluid balance is measured from daily body weight if possible, while hemoglobin and blood electrolytes and creatinine are measured preoperatively and until the fourth postoperative day. Hypovolemic patients are rehydrated with fluid at 20 mL/kg body weight. The unit uses a liberal blood transfusion trigger of 6 mmol/L for the first 4 days postoperatively.

Patients are mobilized as soon as possible after surgery. Physiotherapy is started on postoperative day 1 and continued for 2–5 days during weekdays (for most patients, on a daily basis) until discharge (Kristensen et al. 2016).

Data collection and management

3 of the authors reviewed the medical charts independently, and deaths within 30 days from amputation or during primary hospitalization were classified according to consensus, as: "Definitely unavoidable" being a result of either pre-amputation terminal disease or the patient refusing relevant postoperative care such as nutrition, fluids, and rehabilitation, or "probably unavoidable" being a result of pre-amputation acute life-threatening medical illness with predictable short life expectancy (< 1 month) (Foss and Kehlet 2005). The remaining deaths classified as FTR were defined as those that were related to possible avoidable postoperative complications. We noted whether the patients who died had a notation in their charts on restrictions in the level of active therapy (Foss and Kehlet 2005). Also, the triggering complication of death, based on the medical chart review, was registered. The FTR rate is calculated as patients with 30-day mortality/all patients with a severe postoperative complication (Henneman et al. 2013). The patients classified with "definitively" or "probably" unavoidable deaths were excluded from the FTR calculation. Patients who developed 1 of the following 8 complications while hospitalized were included in the FTR calculation: radiographically verified pneumonia or respiratory failure, sepsis, acute renal failure (postoperative creatinine > 200 μmol/L), stroke, gastrointestinal complication (ileus, hemorrhage), acute myocardial infraction, requirement for more than 3 blood transfusions within 72 hours from surgery, and re-amputation at a higher level within 30 days from index amputation. We were cautious not to register preexisting diseases as postoperative complications. The findings were double-checked by 2 independent researchers.

Statistics

Continuous data are presented as median values with interquartile ranges (IQRs) or mean values with standard deviations (SD). Categorical data are presented as numbers and were compared using the chi-square test or Fisher's exact test in cases with cell counts of 5 or less. Log binominal regression analysis, with 30-day mortality as dependent variable, was used to assess the relative risk of variables with known influence on 30-day mortality (Barros and Hirakata 2003, Kristensen et al. 2012, Karam et al. 2013). The selected variables were: age, sex, ASA score, diabetes, nursing home admission, TFA, and BMI. A corresponding model evaluated the 30-day mortality of FTR patients with active care curtailed, compared with those who survived. Log binominal regression analysis was used due to the relatively few events, thereby eliminating the risk of an overestimation of the estimates from simple multivariable logistic regression analysis (Barros and Hirakata

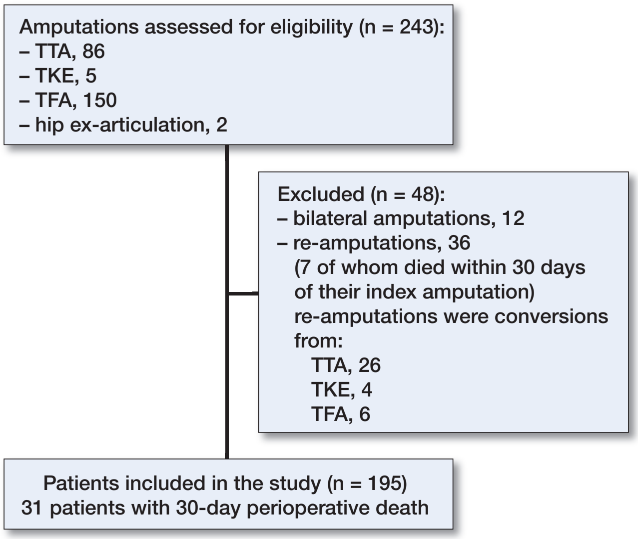

Figure 1. Flow chart of amputee patients at Hvidovre Hospital, from January 2013 to April 2015. TTA = transtibial amputation, TKE = through knee ex-articulation, TFA = transfemoral amputation.

Table 1. Patient characteristics, n = 195. Values are number of patients unless otherwise stated

Factor	Survivors n = 164	Non-survivors n = 31
Male sex	90	19
Female sex	74	12
Age in years, mean (SD)	74 (12)	78 (13)
Own home	110	22
Nursing home	54	9
Body mass index, mean (SD)	24.6 (6.5)	23.5 (6.8)
New mobility score, mean (SD)	3.9 (2.8) [a]	2.5 (3.2) [b]
Diabetes type I or II	68	18
Dementia	22	2
ASA score > 2	135	29
Transtibial amputation	71	9
Through-knee amputation	5	0
Transfemoral amputation	88	22
Intraoperative blood loss (mL), median (IQR)	300 (150–500)	400 (200–675)
General anesthesia	46	9

[a] n = 140.
[b] n = 22.

2003). To our knowledge our study is the first analyzing mortality causality in this group of patients, which is why we were not able to assess variability or distribution before the data collection.

Ethics, funding, and potential conflicts of interest

The study was approved by the local ethics committee and registered with the regional data protection agency (04.12.2012) (j. no. 01975 HVH-2012-053). No benefits in any form have been received or will be received from any commercial party related directly or indirectly to the subject of this article. No competing interests were declared.

Results

195 consecutive patients with a single primary major dysvascular LEA procedure were included in the study between January 2013 and April 2015 (Figure 1 and Table 1).

Causes of death

31 of the 195 patients died in hospital within 30 days after surgery (median of 6 postoperative days (IQR: 4.5–10)): 22 post-TFA procedures and 9 post-TTA procedures (Table 1 and see Supplementary data). There was a statistically significant higher incidence of postoperative sepsis, pneumonia, and acute myocardial infarction among the patients who died compared with the survivors in univariable analysis. In an adjusted log binominal regression analysis TFA and diabetes were associated with an increased risk of 30-day mortality (TFA: RR = 2.3, CI = 1.1–4.8, p = 0.03 and diabetes: RR = 2.7, CI = 1.3–5.6, p = 0.01) (Table 2, see Supplementary data). The 22 patients who died in the TFA sub-group received statistically significantly more blood transfusions during the period from 2 days before surgery and until the fifth postoperative day [median of 3.0 units vs. 2.0 units (p = 0.02)] compared with those 88 patients alive in the TFA group.

Estimation of FTR

4 deaths were classified as "definitely unavoidable," 4 as "probably unavoidable," and 23 as FTR, of which 20 patients at some point had active care curtailed (Table 3). 53 patients experienced at least 1 of the 8 defined complications during their stay at the hospital. The FTR rate was 30% (postoperative complications among all 195 patients may be found in Table 4, see Supplementary data).

Discussion

The 16% 30-day mortality rate in this study is comparable with previous European studies (Moxey et al. 2010) and it shows how severely ill patients are when admitted to the department of orthopedic surgery for a dysvascular-related primary LEA. 84% of the patients had an ASA score of 3–4, most likely the highest within the orthopedic specialty. Patients with diabetes or patients having TFA surgery performed all had an elevated risk of 30-day mortality.

One-quarter of the deaths were highly expected in patients suffering preoperatively from the consequences of septic shock, severe sequelae after recent massive stroke, or unrecoverable respiratory failure. Nevertheless, they had surgery scheduled and performed. This is remarkable and leaves an impression of how selected patients could have a more digni-

Table 3. Classification of patients according to the potential for avoiding death. Values are number of patients unless otherwise stated

Factor	Definitely unavoidable n = 4	Probably unavoidable n = 4	Failure to rescue n = 23	Total n = 31 [a]
Active care curtailed, no/yes	0/4	1/3	3/20	4/27
Estimated cause of death:				
Stroke	0	1	3	4
Acute myocardial infarction	0	0	6	6
Pneumonia or respiratory failure	2	0	5	7
Sepsis	2	2	4	8
Renal failure	0	0	3	3
Gastrointestinal ileus or hemorrhage	0	1	2	3
Postop. days to death, median (IQR)	7 (2.0–9.8)	5 (2.8–6.5)	7 (4.0–11)	6 (4.5–10)

[a] 22 transfemoral and 9 transtibial amputations.

fied death than is the case today if more attention were paid to the possibility of non-surgical palliative treatment. Thus, for some patients, limb ischemia/severe infections along with serious co-morbidities are part of the death process, and a non-surgical approach might be more ethically correct. However, we acknowledge that an algorithm on how to select patients for non-surgical palliative treatment is difficult.

If the mortality rate from postoperative acute myocardial infraction is to be reduced, it seems critical that hypoperfusion is avoided (Dhalla et al. 2010). Clinical estimation alone to guide blood transfusion is probably inadequate (Ram et al. 2014). Daily Hgb measurement is to be recommended, and a close regulation of LEA patients' hemodynamics before and after surgery is important.

Even with a perioperative standard for fluid therapy and antibiotic during surgery, sepsis and pneumonia remain significant challenges. It seems reasonable to consider extending antibiotic prophylaxis into the early postoperative days. Issues such as tissue hypoxia due to surgical stress could be insufficiently monitored on regular wards by blood pressure, heart rate, and saturation only. Different invasive and non-invasive techniques provide an enhanced assessment of optimal oxygen delivery, and individualized goal-directed hemodynamic therapy (Sobol and Wunsch 2011) is perhaps something that needs to be included more often in LEA surgery in the future.

Since our study, to our knowledge, is the first to apply the FTR approach in LEA surgery, it is compared with hip fracture patients with similar demographics. Our patients had an exceptionally high FTR rate. Thus, a US register study on patients with hip fracture published in 2015 with a large patient population reported an FTR rate of 6% (Menendez and Ring 2015). The difference may be explained by different comorbidity patterns.

The fact that 20 of the 23 patients classified as FTR deaths received less than maximum postoperative care gives cause for concern. Doctors curtailed active care on ethical grounds considering the current health status, mental status, and the pre-amputation function level. The decision to curtail active care was taken by the attending medical staff, and not influenced by the authors of this study. Going through the medical records it became evident how the decision not to refer to ICU or active revival was settled. Frequently it was through a conversation between the attending resident and a consultant in the situation of a quickly deteriorating patient. This is stressful and not the ideal time for such discussions.

There are several limitations to this study. The percentage of patients classified as FTR could be too high, and the investigators could have overlooked some complications among the survivors. This could influence the FTR rate and to some extent explain the exceptionally high percentage. The usage of FTR is relatively new and what diagnoses should be included in the calculation is still being debated. A recent study evaluating the concept of FTR found that administrative data are inaccurate in the general hospital population and the FTR rate ought not to be used in its current state for comparative purposes (Horwitz et al. 2007). Another limitation is the retrospective classification of cause of death. However, the final classification was based on the consensus of 3 specialists, including the one responsible for the corresponding hip fracture study (Foss and Kehlet 2005). The data represent the biggest dataset on the subject and provide a background for further exploratory analysis of the subject. The data are partly qualitative, highlighting the fact that there is both a group where care is probably futile as well as a group where postoperative care is probably inadequate. Ideally a future study on this question should be prospective, with independent assessments preoperatively and postoperatively, preferably daily, but at least weekly. From our work and analysis process it became clear that future trials will gain considerably from the recommendations listed in the Appendix.

In summary, the 30-day mortality within this study is comparable to previous studies and shows the potential in continuous research in perioperative strategies. Diabetic patients and patients with TFA have an elevated risk of 30-day mortality. Postoperative sepsis, pneumonia, and acute myocardial infarction are the main complications leading to death following

LEA surgery. It seems apposite to recommend a future intensified focus on the perioperative optimization of LEA patients, and with room for improvements.

Supplementary data

The Appendix and Tables 2 and 4 are available as supplementary data in the online version of this article, http://dx.doi.org/10.1080/17453674.2018.1430420

GH, NBF, and CWI collected the material. CWI, NBF, GH, PTT, AT, and MTK analyzed the data. CWI wrote the first draft and took care of revisions. CWI, PTT, GH, AT, NBF, and MTK contributed to the planning of the study, interpretation of the results, and preparation of the manuscript. The study has not been published and the manuscript is not being considered for publication elsewhere. None of the above-mentioned authors have any conflicts of interest directly related to this study.

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