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Presentation and outcome of critically ill medical and cardiac-surgery patients with acute heart failure

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Summary

Background: The aim of the study was to investigate presentation and outcome of consecutive acute heart failure (AHF) patients admitted to the intensive care unit (ICU) including also patients undergoing cardiac surgery, thereby providing comparative information on all critically ill AHF subgroups.

Methods: The prospective observational study with 6-month follow up was performed in the cardio-thoracic and the medical ICU of a university hospital. AHF was defined according to the European Society of Cardiology guidelines. Univariate Cox regression was used to calculate hazard ratio (HR) and 95% confidence intervals (CI) for risk factors.

Results: A total of 192 patients fulfilled the AHF criteria, of whom 86 and 24 underwent elective and emergency cardiac surgery, respectively. The remaining 82 medical patients had no surgical interventions. Cardiogenic shock was diagnosed in 32% of all patients and was the most common AHF presentation. Medical, elective surgery and emergency surgery AHF patients had a mortality at 30 days of 31%, 4.7% and 22% ($p < 0.05$) and at 180 days of 42%, 6.1% and 23% ($p < 0.05$), respectively. While the presence of cardiogenic shock was associated with a poor outcome (HR 1.8, CI 1.0–3.0; $p = 0.04$), post-operative cardiac stunning had a good prognosis (HR 0.06, CI 0.01–0.47; $p < 0.01$). Mortality worsened when infections (HR 2.8, CI 1.5-5.7; $p < 0.01$) or renal dysfunction (HR 4.4, CI 2.2–8.4, $p < 0.01$) were present on ICU admission.

Conclusions: Medical patients, patients undergoing elective cardiac surgery and patients requiring emergency cardiac surgery are three distinct AHF-subpopulations. Co-morbidities and surgical treatment options affect long-term outcome.

Key words: acute heart failure; cardiogenic shock; cardiac surgery; intensive care unit; mortality

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Introduction

Acute heart failure (AHF) is a common clinical entity associated with a high morbidity and mortality [1–4]. When the AHF symptoms become so severe that affected patients require continuous monitoring and organ support, medical management is usually provided in the intensive care unit (ICU). Many AHF patients will further need emergency cardiac surgery during the course of their illness. Others develop AHF symptoms after undergoing elective cardiac surgery. However, only one study provides details on ICU patients with AHF [5], while others do not specifically comment on patients hospitalised in the ICU [6–10]. A limitation common to all these epidemiological studies is that they do not particularly report on the subgroup of AHF patients requiring cardiac surgery.

List of abbreviations

ACE	angiotensin converting enzyme
AHF	acute heart failure
CI	confidence interval
HR	hazard ratio
ICU	intensive care unit

The aim of this study was to provide comparative information on a broad range of AHF syndromes in critically ill patients, including those undergoing cardiac surgery. We therefore assessed population characteristics of consecutive AHF patients admitted to the medical and cardiosurgical ICU. In addition, we investigated short and long-term outcome of our critically ill AHF population and assessed risk factors influencing mortality.

Methods

Study population

We conducted a prospective observational study, using an identical evaluation protocol, at the 12-bed medical ICU and at the 10-bed cardiac surgery ICU of the University Hospital Zurich, Switzerland. Consecutive patients were screened for the diagnosis of AHF on the day of their ICU admission. Patients were included in the analysis only once, even if they were readmitted during the observation period. The study was carried out in compliance with the Helsinki Declaration. Patients and/or their relatives gave their oral informed consent for the anonymous analysis of the collected routine clinical and laboratory data. The Institutional Review Board waived the need for written informed consent in this particular instance.

Diagnosis of acute heart failure

AHF is defined as the rapid onset of symptoms and signs secondary to abnormal cardiac function, which is described as the inability to pump sufficient blood at normal end-diastolic pressures. Our classification was adapted from the AHF guidelines provided by the European Society of Cardiology and the European Society of Intensive Care Medicine [11]. We included the following distinct clinical conditions:

- Cardiogenic shock: Low cardiac output (<2.2 l/min/m^2) with or without low BP after correction of preload, with evidence of tissue hypoperfusion or organ dysfunction.
- Post-operative cardiac stunning: Transient and reversible impairment of contractility after cardiac surgery, resulting in low cardiac output after correction of preload, with need for inotropic support in order to prevent tissue hypoperfusion and organ dysfunction.
- Pulmonary oedema: Heart failure induced severe respiratory distress, accompanied by crackles over both lungs and bilateral infiltrates in the chest X-ray.
- Congestive heart failure: All other conditions with AHF signs and symptoms, which do not fulfill the diagnostic criteria for the AHF syndromes described above, e.g. during the observation period after myocardial infarction. No particular distinction between left-, right-, and biventricular failure was undertaken.

In addition, we identified patients with sepsis-induced cardiac dysfunction, which required inotropic support due to an impaired left ventricular ejection fraction or low cardiac output. It is important to note that we did not diagnose AHF by elevated natriuretic peptide levels alone as it has been shown that these markers have a limited specificity in critically ill patients [12–14].

Case definition

AHF patients were divided into surgical and medical sub-groups, whether or not they had heart surgery preceding or during the ICU stay. Surgical patients were divided in two groups whether they underwent elective surgery or emergency (= non-elective) operations. Myocardial infarction (MI) was diagnosed in the presence of coronary artery disease, typical ECG changes and elevated (≥0.1 mg/l) troponin T levels. Clinical and laboratory data were recorded on the day of ICU admission. Like in the Euro Heart Failure Survey II, renal dysfunction was defined as serum creatinine levels >177 mmol/l (>2 mg/dl) [7]. Data for the Simplified Acute Physiology Score II (SAPS II) were collected as the worst value within 24 hours after ICU-admission [15]. Left ventricular ejection fraction was determined by echocardiography or ventriculography 24 hours prior or during the ICU stay.

Statistics

Group comparison for continuous variables was tested with the Mann Whitney U test and categorical variables were compared with the chi-square test. Survival estimates for all cause mortality were calculated with the method of Kaplan and Meier. The Log Rank test was used to compare the mortality subgroups. Hazard ratio (HR) and 95% confidence intervals (CI) for risk factors influencing mortality were calculated with a univariate Cox regression model. All tests were performed with the use of SPSS 11.0.4 for Mac OS X.

Results

Patient characteristics

During the 3-month observation period 355 consecutive ICU-admissions were screened for the diagnosis of AHF. One hundred and seventy-two patients out of 355 (48%) were treated without surgery and classified as medical patients. Of the 172 medical patients 82 (48%) fulfilled the diagnosis of AHF. One hundred and eighty-three of 355 (52%) patients underwent cardiac surgery and were classified as surgical patients, and AHF was diagnosed in 110/183 (61%). Of the 110 surgical patients 86 (78%) underwent elective cardiac surgery and 24 (22%) required emergency cardiac surgery.

Baseline characteristics for the three groups of AHF patients are shown in table 1. A history of chronic heart failure was present in 34% of medical patients, 57% of patients undergoing elective cardiac surgery and 4.2% of patient requiring emergency cardiac surgery (p <0.01 between

groups). Cardiac operations were performed under extracorporeal circulation (ECC) in 90/110 (82%) surgical patients. Coronary artery bypass grafting, the most frequent operation, was performed in 50% of surgical AHF patients. Other surgical procedures included aortic valve replacement (24%), mitral valve repair (15%), mitral valve replacement (5.5%), and pericardial drainage (4.5%). Five patients (4.5%) received a left ventricular assist device or a heart transplant prior or during their ICU stay. Regarding these frequencies, no differences were found between elective and emergency surgery patients. Major vascular surgery was performed alone in 6.4% and combined with heart surgery in 8.2% of surgical AHF patients. On ICU admission, inotropes were used significantly more often ($p < 0.01$) in elective surgery (63%) and emergency surgery patients (54%) than in medical (21%) patients. Similarly, vasopressors were required significantly ($p < 0.01$) more often in elective surgery (70%) and emergency surgery (63%) patients than in medical patients (33%).

Table 2 shows the frequencies of the different AHF syndromes as well as values of selected clinical and laboratory parameters. Surgical patients pre-treated with beta-blockers, ACE-inhibitors or angiotensin II-antagonists did not present more frequently with low output syndrome or shock than patients without medical pre-treatment. Organ dysfunction for the three groups is displayed in table 3. Left ventricular ejection fraction was 40 (10–75)% and not statistically different between the three groups. SAPS II was 31 (6–84) in medical patients and 22 (6–52) in elective surgery patients with a significant difference between the two groups ($p < 0.01$). Patients undergoing emergency surgery had SAPS II of 27 (12–84), which was also significantly higher compared to the scores of patients undergoing elective cardiac surgery ($p < 0.01$).

Outcome and risk factors

Length of ICU stay was significantly shorter in medical patients (3 (1–30) days; $p < 0.01$) and in elective surgery patients (3 (1–83) days; $p < 0.01$) than in emergency surgery patients (6.5 (2–38) days). The average length of hospital stay though was 11 (2–170) days and not different between the three groups. Survival curves for the three AHF populations are displayed in figure 1. Medical, elective surgery and emergency surgery AHF patients had a mortality at 30-days of 31%, 4.7% and 22% ($p < 0.05$) and at 180-days of 42%, 6.1%

Table 1
Baseline characteristics.

	Medical AHF-patients (n = 82)	AHF patients with elective surgery (n = 86)	AHF-patients with emergency surgery (n = 24)	p-value (medical vs elective surgery)	p-value (medical vs emergency surgery)	p-value (elective vs emergency surgery
Patient characteristics:						
Age (years) – median (range)	66 (30-96)	67 (18-85)	59 (28-84)	0.985	0.349	0.352
Male sex	55 (67%)	56 (65%)	20 (83%)	0.871	0.201	0.133
Underlying cardiac disease:						
Coronary artery disease	57 (70%)	53 (62%)	12 (50%)	0.331	0.092	0.352
Cardiac valve disease	15 (18%)	47 (55%)	11 (46%)	**<0.001**	**0.013**	0.494
Hypertensive cardiomyopathy	8 (9.8%)	15 (17%)	1 (4.2%)	0.180	0.680	0.187
Dilated cardiomyopathy	7 (8.5%)	8 (9.3%)	2 (8.3%)	1.000	1.000	1.000
Precipitating factors:						
STEMI	26 (32%)	3 (3.5%)	3 (13%)	**<0.001**	0.073	0.117
Non-STEMI	16 (20%)	28 (33%)	6 (25%)	0.079	0.574	0.619
Systolic BP >150 mm Hg	9 (11%)	3 (3.7%)	1 (4.3%)	0.131	0.687	1.000
Infection on ICU-admission	20 (24%)	0 (0.0%)	6 (25%)	**<0.001**	1.000	**<0.001**
Underlying diseases:						
Systemic arterial hypertension	36 (44%)	43 (50%)	16 (67%)	0.444	0.064	0.171
Diabetes mellitus	22 (27%)	11 (13%)	3 (13%)	**0.032**	0.180	1.000
Chronic lung disease	9 (11%)	19 (22%)	1 (4.2%)	0.064	0.450	0.069
Drug history:						
Betablockers	31 (38%)	54 (63%)	6 (25%)	**0.002**	0.332	**0.001**
ACE inhibitors	24 (29%)	43 (51%)	7 (29%)	**0.007**	1.000	0.069
AT II inhibitors	10 (12%)	10 (12%)	2 (8.3%)	1.000	0.730	1.000
Statins	27 (33%)	43 (50%)	4 (17%)	**0.029**	0.201	**0.005**
Diuretics	34 (42%)	44 (51%)	8 (33%)	0.220	0.636	0.166
Aldactone	11 (13%)	14 (16%)	0 (0%)	0.668	0.066	**0.037**

Age is displayed as median (range), all other values represent number of patients (percentage of patients). STEMI denotes ST-elevation myocardial infarction, BP blood pressure, ACE angiotensin converting enzyme, and AT angiotensin.

and 23% (p <0.05), respectively. Figure 2 shows survival curves for the various AHF syndromes. Cardiogenic shock was associated with an unfavourable outcome (HR 1.8, CI 1.0–3.0; p = 0.04), particularly in medical patients, who had a 180-day mortality of 72% (compared to 20% in surgical patients; p <0.01). In contrast, post-operative cardiac stunning had a good prognosis (HR 0.06, CI 0.01–0.47; p <0.01). Six patients had sepsis-induced myocardial depression, and only 3 (50%) of them were still alive at 6 months. Infections on admission generally increased the risk of death (HR 2.8, CI 1.5–5.7; p <0.01). Mortality was lower in patients pre-treated with beta-blockers (HR 0.5, CI 0.3–1.0; p = 0.04) and statins (HR 0.4, CI 0.2–0.8; p = 0.01), while the use of ACE inhibitors was not associated with any statistically significant effect.

Table 2

Clinical presentation of AHF.

	Medical AHF-patients (n = 82)	AHF patients with elective surgery (n = 86)	AHF-patients with emergency surgery (n = 24)	p-value (medical vs elective surgery)	p-value (medical vs emergency surgery)	p-value (elective vs emergency surgery
AHF syndromes:						
Cardiogenic shock	18 (22%)	28 (33%)	16 (67%)	0.166	**<0.001**	**0.004**
Pulmonary oedema	25 (31%)	1 (1.2%)	1 (4.2%)	**<0.001**	**0.012**	0.390
Congestive heart failure	33 (40%)	18 (21%)	5 (21%)	**0.007**	0.093	1.000
Post-operative cardiac stunning	0 (0.0%)	39 (45%)	2 (8.3%)	**<0.001**	0.051	**0.001**
Sepsis-induced cardiac depression	6 (7.3%)	0 (0.0%)	0 (0.0%)	**0.012**	0.333	–
Parameters on ICU admission:						
Respiration rate (1/min)[A]	20 (12–60)	13 (10–30)	15 (9–35)	**<0.001**	**0.021**	**0.004**
Heart rate (1/min)	85 (30–180)	88 (32–120)	92 (50–140)	0.664	0.737	0.403
Mean arterial BP (mm Hg)	80 (42–180)	70 (50–110)	75 (50–100)	**0.025**	0.337	0.687
CVP (mm Hg)[B]	12 (2–22)	9 (1–17)	10 (5–26)	**0.002**	0.987	0.060
Urine output (ml/h)[C]	60 (0–480)	115 (0–340)	90 (0–200)	**<0.001**	0.137	**0.034**
Laboratory parameters:						
Haemoglobin (g/l)	118 (55-197)	96 (31-175)	99 (75–175)	**<0.001**	**0.045**	0.506
Leukocyte count (1/µl)	11245 (790–54790)	8500 (3670–20870)	9655 (4670–27950)	**<0.001**	0.234	0.155
Troponin (µg/l)[D]	0.31 (0.01–24)	0.29 (0.01–2.7)	0.32 (0.01–27)	0.198	0.900	0.584
NT-proBNP (ng/l)[E]	4337 (138–70000)	2371 (390–13'702)	4934 (1000–33335)	0.080	0.712	**0.022**
C-reactive protein (mg/l)[F]	28 (1.0–316)	11 (1.0–136)	52 (5.0–365)	**0.012**	0.052	**<0.001**
Creatinine (µmol/l)[G]	102 (57–2277)	82 (49–144)	111 (57–567)	**<0.001**	0.571	**<0.001**

Values represent number (percentages) or median (range). BP denotes blood pressure, CVP central venous pressure, and NT-proBNP N-terminal pro B-type natriuretic peptide. Values for calculations were available in [A] 62 (not intubated), [B] 135, [C] 173, [D] 184, [E] 97, [F] 176 and [G] 185 patients.

Table 3

Organ dysfunction.

	Medical AHF-patients (n = 82)	AHF patients with elective surgery (n = 86)	AHF-patients with emergency surgery (n = 24)	p-value (medical vs elective surgery)	p-value (medical vs emergency surgery)	p-value (elective vs emergency surgery
Cardiovascular dysfunction:						
Mean arterial BP <65 mm Hg	14 (17%)	14 (17%)	6 (25%)	1.000	0.390	0.375
Cardiac index ≤2.2 l/min/m^2 [A]	4 (33%)	33 (50%)	5 (42%)	0.356	1.000	0.756
LV ejection fraction <40%[B]	14 (48%)	12 (24%)	5 (36%)	**0.046**	0.523	0.495
Respiratory dysfunction:						
Arterial pO_2/FiO_2 <300 mm Hg[C]	42 (78%)	30 (40%)	13 (65%)	**<0.001**	0.369	**0.047**
Renal dysfunction:						
Creatinine >177 µmol/l (>2.0 mg/dl)[D]	18 (23%)	0 (0.0%)	3 (13%)	**<0.001**	0.390	**0.011**
Metabolic dysfunction:						
Glucose ≥11.1 mmol/l [E]	14 (18%)	4 (4.9%)	4 (17%)	**0.011**	1.000	0.076

Values represent number of patients (percentage of patients). BP denotes blood pressure, LV left ventricular, paO_2/FiO_2 arterial partial pressure of oxygen per fraction of inspired oxygen. Values for calculations were available in [A] 90, [B] 93, [C] 150, [D] 185 and [E] 183 patients.

Figure 1

The Kaplan Meier curves show survival rates for three groups of ICU-patients with acute heart failure over time, starting at the day of ICU admission. The small vertical lines indicate the time points when patients had their last follow up. The survival curves between the three groups were significantly different (Log Rank p <0.001).

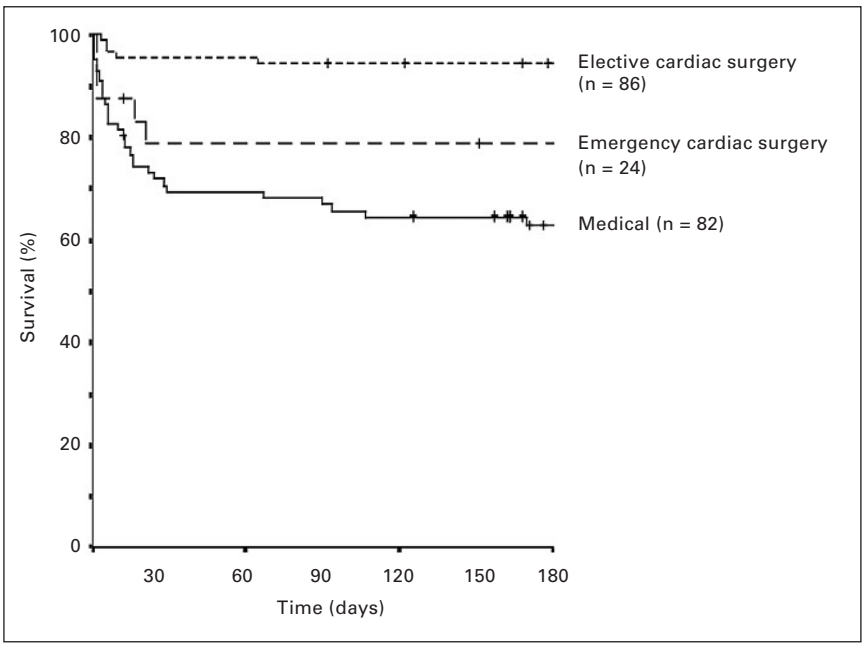


Figure 2

The Kaplan Meier curves show survival rates of ICU-patients with different acute heart failure syndromes over time, starting at the day of ICU admission. The small vertical lines indicate the time points when patients had their last follow up. The survival curves between the groups were significantly different (Log Rank p <0.001). The 6 patients with sepsis-induced myocardial depression are not included in this graph.

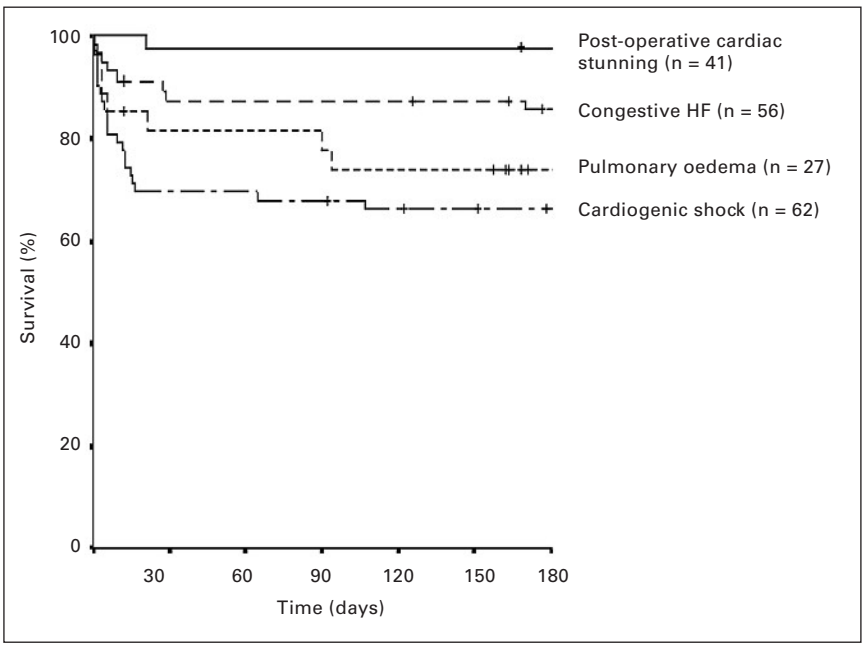
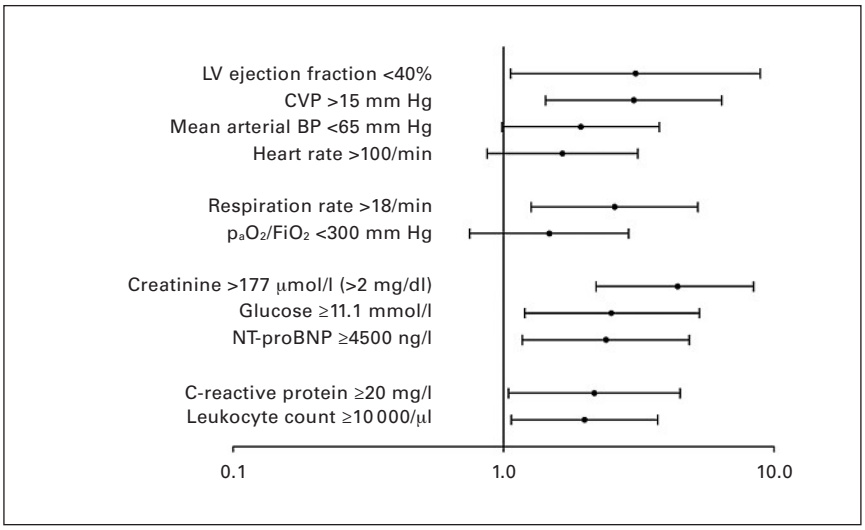


Figure 3

Univariate risk factors for mortality. Bars represent hazard ratios with 95% confidence intervals. A value >1.0 indicates an increased risk of mortality, a value <1.0 denotes a risk reduction. Bars crossing 1.0 do not reach statistical significance. LV denotes left ventricular, CVP central venous pressure, BP blood pressure, p_aO_2/F_iO_2 arterial partial pressure of oxygen per fraction of inspired oxygen, and NT-proBNP N-terminal pro B-type natriuretic peptide.



Discussion

The present study investigated consecutive AHF patients admitted to the ICU including also patients undergoing cardiac surgery, thereby providing for the first time comparative information on all critically ill AHF subgroups. Our results demonstrate that medical patients, patients undergoing elective cardiac surgery and patients requiring emergency cardiac surgery are three distinct AHF-subpopulations. Co-morbidities, organ dysfunction, and surgical treatment options determined long-term outcome. The following sections elucidate important differences between medical and cardio-surgical patients and put them into context with the risk of death.

Patient characteristics

In our ICU study population mortality was highest in medical AHF patients. A similar 4-week mortality (27%) was found in a multi-centre survey investigating 581 ICU patients in whom experts diagnosed acute decompensated heart failure from the patients' charts [5]. However, 33% of these patients had a history of cardiac surgery and/or percutaneous coronary intervention, but this sub-population was not analysed separately. In our medical patients AHF was most frequently a de novo diagnosis. This stands in contrast to a general heart failure population in which de novo AHF was diagnosed in only one third of the patients [1]. Pulmonary oedema and congestive heart failure were the most common presentations in medical AHF patients. Sepsis-induced cardiac depression was responsible only for a minority of AHF cases and accompanied by a poor outcome.

Elective surgery patients had the lowest mortality. Firstly, they were more commonly pretreated with beta-blockers and statins. This reflects optimised treatment prior to elective surgery. Secondly, surgical patients more frequently had a valvular pathology as the underlying cardiac disease, amenable to surgical treatment. Furthermore, elective cardiac patients had no infections on ICU admissions and the lowest rate of renal dysfunction. Finally, elective surgery patients presented frequently with post-operative cardiac stunning. Underlying mechanisms include reversible myocardial depression due to inflammatory activation after extracorporeal circulation and surgical trauma, anaesthetic medication, and transient hypothermia.

Precipitating factors and interventions

Elevated laboratory parameters of inflammation were related to increased mortality which supports recent studies investigating the use of C-reactive protein levels [16] or leukocyte counts in AHF patients [17]. It has been suggested that an activation of the inflammatory cascade contributes to the pathophysiology of heart failure [18]. The question remains how much infections contribute to the observed rise in inflammatory markers in this condition. In our study, clinically evident infections on ICU admission had a negative impact on mortality. As infections further depress cardiac function [19] more research is needed to understand the interaction between heart failure and infections.

While elective surgery was accompanied by a low risk of death, mortality increased when patients had to undergo emergency surgery. Typical indications for emergency surgery included repair of mechanical complications after myocardial infarction and bypass grafting in patients not suitable for a percutaneous coronary intervention. Intravenous drug treatment with inotropes was more frequent in surgical patients than in medical patients. In fact, many surgical patients required inotropes during surgery and in their first hours after ICU admission due to a low cardiac output. In patients undergoing elective cardiac surgery, inotropes were frequently administered to prevent tissue hypoperfusion and organ dysfunction. These patients were classified as post-surgical cardiac stunning, which is a particular form of AHF generally associated with a rapid improvement and a low mortality. In patients requiring emergency surgery, however, inotropes were frequently needed to treat cardiogenic shock accompanied by organ dysfunction.

Organ dysfunction

Patients with cardiogenic shock had a high mortality. However, their overall 180-day mortality of less than 40% was lower than in earlier studies performed in general [1, 2, 7] and ICU patients [5] with AHF. This is because the majority of cardiogenic shock patients included in the present study had a surgical treatment option. In medical patients, the relationship between low systolic blood pressure and poor prognosis has previously been reported [10, 20]. A creatinine serum level >177 mmol/l indicating renal function impairment was associated with an adverse outcome, too. This result supports previous findings that renal dysfunction has a negative impact on survival in AHF patients and in patients undergoing cardiac surgery [1, 21–23].

Limitations of the study

It is important to note, that AHF was diagnosed on ICU admission. Some surgical patients had their operation before ICU admission (usually elective cardiac surgery). Others were admitted to the ICU first and had their operations later in the ICU course (usually emergency cardiac surgery). Our observational study was designed to monitor diagnostic procedures and treatments of AHF-patients in our institution. Hence, some laboratory values are lacking because the treating physician did not consider them to be necessary for the management of the patient. Similarly, echocardiography was not routinely performed while the patients were hospitalised in the ICU. Other parameters such as blood pressure or cardiac output are clearly influ-

enced by ongoing treatment and must be interpreted with caution. We used multiple univariate testing for the exploration of differences between groups and for possible risk factors influencing mortality. Although useful for hypothesis generation, this approach increases the risk of type 1 errors and might explain differences to other studies. Larger studies are needed to investigate complex interactions between risk factors.

Conclusions

This prospective observational study performed in a medical and cardio-surgical ICU confirms that medical patients, patients with elective surgery and patients with emergency surgery are three distinct AHF-populations. Co-morbidities, organ dysfunction, and surgical treatment options affect their mortality. The results of this study provide essential background information for larger multi-centre studies and future therapeutic trials in critically ill patients with AHF.

Authors' contributions

AR designed the study, collected and analysed the data, and drafted the manuscript. FB and MS collected and analysed the data. ES, MM and FF designed the study, analysed the data and drafted the manuscript. All authors read and approved the final version of the manuscript.

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