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Risk factors associated with new onset tachyarrhythmias after cardiac surgery – a retrospective analysis

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Background: Tachyarrhythmias (TA) represent a frequent and serious problem after cardiac surgery. We retrospectively analyzed 987 cardiac surgery patients admitted to a surgical intensive care unit between 1996 and 1999 to assess incidence and risk factors associated with development of postoperative TA in the intensive care unit.

Methods: TA (n=149) were defined as non-sinus rhythm with a heart rate (HR) ≥100 bpm in patients with preoperative sinus rhythm or as heart rate ≥130 bpm in patients with preoperative atrial fibrillation. A total of 787 patients served as controls (C). Demographic, premorbidity and perioperative data, admission SAPS and MODS-score, presence of clinical syndromes systemic inflammatory response syndrome (SIRS) and sepsis were univariately compared between groups. For prediction of independent risk factors for TA-development two multiple logistic regression models were finally established.

Results: Concerning TA, atrial fibrillation and flutter (76%) were observed most frequently, followed by paroxysmal supraventricular tachycardia (15%) and ventricular tachycardia/fibrillation (11%). Age, a history or presence of congestive heart failure, development of SIRS and sepsis, severity of multiple organ dysfunction syndrome and in particular severity of cardiovascular failure proved to be independent risk factors for development of TA.

Conclusion: In cardiac surgery patients, age, a history or presence of congestive heart failure, postoperative development of a systemic inflammatory response syndrome or sepsis and the severity of multiple organ function syndrome were independent predictors for development of TA in the intensive care unit. The association of severity of cardiovascular dysfunction with TA strongly suggests a causal relationship between catecholamine therapy and TA-development.

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Key words: Tachyarrhythmia; cardiac surgery; intensive care; MODS; SIRS; sepsis; catecholamines.

TACHYARRHYTHMIAS (TA) are a frequent and important clinical problem in cardiac surgery patients during the postoperative period. TA often cause hemodynamic instability necessitating initiation or prolongation of catecholamine therapy for hemodynamic stabilization and resulting in an extended intensive care unit stay and an increased duration of hospitalization (1). In addition, TA have been reported to increase intensive care and hospital mortality and significantly increase hospital costs (2, 3).

The reported incidence of TA in patients undergoing cardiac surgery varies between 10% and approximately 50%. However, little is known about the exact cause of postoperative TA and reports concerning risk factors associated with their development have yielded heterogeneous results (1). Most authors have focused on the influence of preoperative demographic data, premorbidity and intraoperative risk factors for subsequent development of TA while the impact of postoperative events and treatment has largely been ignored.

In this study we retrospectively analyzed 987 cardiac surgery patients from our database in order to evaluate incidence and risk factors associated with development of postoperative TA in the intensive care environment. Using a multiple logistic regression analysis, we searched for significant preoperative, perioperative and in particular postoperative predictors for development of TA in cardiac surgery patients.

Methods

The study was institutionally approved as a retrospective investigation. We analyzed database files of all cardiac surgery patients (n=987) admitted to a general and surgical intensive care unit (ICU) between January 1996 and September 1999. All cardiac pro-

cedures were performed using a continuous midazolam/fentanyl intravenous anesthesia. Monitoring consisted of an arterial pressure line, continuous ECG recording and in the majority of patients a pulmonary artery catheter and transesophageal echocardiography. After institution of cardiopulmonary bypass patients were cooled to 32–34°C core temperature using alpha-stat management. During cardiopulmonary bypass target mean arterial pressures were set between 50 and 60 mmHg by increases or decreases of pump flow and use of vasopressors if necessary. Cold crystalloid (St. Thomas) or blood cardioplegia was infused in an antegrade fashion. Retrograde cardioplegia was applied in selected cases. For valve surgery topical ice slush was used for additional cooling of the heart.

Patients developing TA during their ICU stay were enrolled into a tachyarrhythmia group (TA; n=149) while patients without TA (C; n=787) served as controls. Patients developing sinus tachycardia in the ICU (n=51) were excluded from statistical analysis. TA were defined as non-sinus rhythm with a heart rate (HR) ≥100 bpm in patients with preoperative sinus rhythm or as heart rate ≥130 bpm in patients with preoperative atrial fibrillation. Patients developing more than one episode of TA were included into analysis only at their first episode. The following data were collected from all patients.

Demographic data included age, sex, preoperative left ventricular ejection fraction (EF) and preoperative cardiac rhythm. Simplified Acute Physiologic Score (SAPS) was calculated for all patients based on worst physiological data obtained within the first 24 h after ICU admission (4). Calculated SAPS was modified by subtracting age points (=SAPSc) because age was separately introduced into the statistical analysis. In patients developing TA within the first 24 h (n=32), SAPSc was calculated from worst data obtained before onset of TA.

Premorbidity factors included history of coronary artery disease, myocardial infarction within the last six months, congestive heart failure, hypertension, diabetes, pre-existing renal insufficiency, and chronic obstructive pulmonary disease. *Premorbidity factors* were recorded in a binary fashion (1=presence or history of a defined premorbid condition; 0=no specified disease).

Perioperative data included type of surgery (emergency, elective), time on cardiopulmonary bypass, aortic cross-clamp time, and specific surgical procedures: aortocoronary bypass, aortic valve surgery, mitral valve surgery, aortic and mitral valve surgery, valve surgery and aortocoronary bypass, miscellaneous cardiac surgical procedures.

In TA patients, a modified multiple organ dysfunction syndrome (MODS)-score was calculated from worst physiologic data before onset of tachyarrhythmia (5; Appendix I). Organ dysfunction was assessed only for pulmonary, liver, renal, hematological and cardiovascular systems because for these organ systems function can be defined on simple laboratory examinations and clinical data. Concerning the central nervous system, all patients exhibited normal Glasgow Coma Scale before surgery and most patients were analgosedated at onset of TA. In addition no patient developed overt gastrointestinal bleeding during the study but moderate gastrointestinal dysfunction cannot be excluded by simple clinical examination. In controls, the highest daily MODS-score during ICU stay was used for statistical comparison.

TA patients were evaluated for the presence or absence of the clinically defined syndromes of systemic inflammatory response syndrome (SIRS) and sepsis specifically during 24 h before onset of TA (6; Appendix II). SIRS and sepsis were combined for statistical analysis because in the clinical situation an infectious cause of SIRS can often not been ruled out on the basis of radiological and bacteriologic findings. In controls, presence or absence of SIRS and sepsis was evaluated daily during the whole ICU stay. The presence of defined clinical syndromes was recorded in a binary fashion (1=presence of SIRS or sepsis with a defined infectious focus or microbiological proven bacteremia; 0=no clinical syndrome).

Routine tachyarrhythmia workup in our ICU includes: 12-lead ECG, arterial blood gas/serum electrolyte analysis and serial CK-MB isoenzyme measurements. Additionally, serum levels of digoxin or digitoxin were measured in patients on chronic medication with cardiac glycosides. Concerning preoperative cardiovascular drugs, only betablocker treatment is normally continued during the peri- and postoperative period in cardiac surgery patients. We do not use any standard prophylactic drug treatment to prevent postoperative arrhythmias.

Demographic data, SAPSc-score, premorbidity factors, perioperative data, MODS-score, presence of SIRS or sepsis were compared with the use of Student's *t*-test, Chi^2-test, or Mann-Whitney U-rank sum test, as appropriate. All variables univariately associated with TA were entered into two multiple logistic regression models. In the first model the overall MODS-score was multivariately analyzed. For the second model MODS-score was spliced into single organ systems, allowing an analysis of severity of individual organ dysfunction combined with its associated therapeutic effort for stabilization on development of TA. Adjusted odds ratios and 95% confidence intervals

were calculated to represent the relative risk of the predictive variables. *P*-values ≤0.05 were considered statistically significant. Data are presented as means±standard deviations (SD).

Results

Of 987 cardiac surgery patients, 149 (15%) developed postoperative TA in the ICU. Atrial fibrillation and atrial flutter were observed most frequently (113/987; 11.4%), followed by paroxysmal supraventricular tachyarrhythmias (22/987; 2.2%) and ventricular tachycardia/ventricular fibrillation (16/987; 1.6%). Thirty-two patients developed TA within 24 h after ICU admission. Serum potassium concentrations were within normal laboratory limits in all TA patients (mean±SD: 4.1±0.36). In patients receiving cardiac glycosides, serum glycoside concentrations were within normal limits.

Table 1 presents results of univariate analysis concerning demographics, premorbidity factors, perioperative data, SAPSc, MODS-score and presence or absence of SIRS and sepsis in patients with and without development of TA. TA patients were significantly older, had a higher incidence of pre-existing congestive heart failure, COPD, renal failure and a significantly lower left ventricular ejection fraction before surgery. Emergency procedures, surgery involving the mitral valve, combined coronary artery and valve procedures and prolonged bypass and aortic cross-clamp times were univariately associated with development of TA. Moreover, patients developing TA exhibited a greater degree of physiologic derangement at admission (SAPSc) and developed more severe organ dys-

Table 1

Demographic, premorbidity and perioperative scoring data and incidence of SIRS and sepsis in patients with and without TA.

	TA n (%); mean±SD	C n (%); mean±SD	*P*-value
N	149	787	
Demographic data			
male	89 (14.0)	545 (86.0)	
female	60 (19.9)	242 (80.1)	
age (years)	67.3±10.0	63.5±11.3	*P*<0.001
preoperative sinus rhythm	137 (92)	760 (96.6)	*P*=0.01
Premorbidity data			
arterial hypertonie	97 (65.1)	506 (64.3)	*P*=0.926
diabetes mellitus	33 (22.1)	151 (19.2)	*P*=0.431
coronary heart disease	113 (75.8)	635 (80.7)	*P*=0.182
myocardial infarction (last 6 months)	31 (20.8)	122 (15.5)	*P*=0.116
congestive heart failure	76 (51.0)	155 (19.7)	*P*<0.001
ejection fraction (%)	49.8±15.6	56.1+15.0	*P*<0.001
COPD	63 (42.3)	215 (27.3)	*P*<0.001
renal failure	36 (24.2)	85 (10.8)	*P*<0.001
Perioperative data			
elective surgery	123 (82.6)	762 (96.8)	*P*<0.001
emergency surgery	25 (16.8)	25 (3.8)	*P*<0.001
ACBP	69 (46.3)	521 (66.2)	*P*<0.001
AVS	24 (16.1)	134 (17.0)	*P*=0.905
MVS	16 (10.7)	29 (3.7)	*P*=0.001
AVMVS	8 (5.4)	6 (0.8)	*P*< 0.001
VSACBP	18 (12.1)	38 (4.8)	*P*=0.002
MS	14 (9.4)	59 (7.5)	*P*=0.408
bypass time (min)	138.5±78.4	101.2±40.9	*P*<0.001
aortic cross-clamp time (min)	73.2±38.4	53.2±26.3	*P*<0.001
Scoring systems:			
SAPSc	10.6±4.1	7.9±3.4	*P*<0.001
MODS	4.9±3.1	1.5±2.0	*P*<0.001
SIRS/sepsis	74 (49.7)	60 (7.6)	*P*<0.001

TA – tachyarrhythmia patients; C – control patients; COPD – chronic obstructive pulmonary disease; ACBP – aortocoronary bypass surgery; AVS – aortic valve surgery; MVS – mitral valve surgery; AVMVS – aortic and mitral valve surgery; VSACBP – valve surgery and aortocoronary bypass; MS – miscellaneous cardiac procedures; SAPSc – Simplified Acute Physiologic Score corrected for age points; MODS – Multiple Organ Dysfunction Syndrome including pulmonary, liver, renal, hematological and cardiovascular organ system; SIRS – Systemic Inflammatory Response Syndrome.

Table 2

Results of multivariate logistic regression analyses.

	TA n (%); mean±SD	C n (%); mean±SD	Adjusted Odds Ratio	Odds Ratio (95% CI)	*P*-value
N	149	787			
1st model:					
age	67.3±10.0	63.5±11.3	1.02/year	1.00–1.04	$P=0.038$
congestive heart failure	76 (51.0)	155 (19.7)	2.67	1.73–4.12	$P<0.001$
SIRS/Sepsis	74 (49.7)	60 (7.6)	2.14	1.11–4.12	$P=0.024$
MODS-score	4.9±3.1	1.5±2.0	1.37/point	1.24–1.52	$P<0.001$
2nd model:					
age	67.3±10.0	63.5±11.3	1.02/year	1.00–1.05	$P=0.022$
congestive heart failure	76 (51.0)	155 (19.7)	2.78	1.81–4.24	$P<0.001$
SIRS / Sepsis	74 (49.7)	60 (7.6)	3.54	2.11–5.94	$P<0.001$
moderate cardiovascular failure	40 (26.8)	135 (17.1)	4.37	2.52–7.59	$P<0.001$
severe cardiovascular failure	83 (55.7)	91 (11.6)	7.88	4.38–14.17	$P<0.001$

MODS – Multiple Organ Dysfunction Syndrome including pulmonary, liver, renal, haematological and cardiovascular organ systems; SIRS – Systemic Inflammatory Response Syndrome.

function in the ICU. In contrast to control patients almost 50% of TA patients fulfilled criteria of SIRS or sepsis in the ICU.

ICU mortality in patients developing TA was significantly higher (25/149; 16.8%; $P<0.001$) when compared with control patients (21/787; 2.7%), although no patient in the TA group died as direct consequence of TA. In addition, TA patients stayed significantly longer in the ICU (8.6±9.2 days; $P<0.001$) when compared with controls (2.6±2.1 days).

Results of multivariate logistic regression analysis are presented in Table 2. Age, a history or presence of congestive heart failure before surgery, development of SIRS and sepsis and severity of MODS proved to be independent risk factors for development of TA. When MODS-score was divided into different organ systems, only degree and severity of cardiovascular failure remained a significant independent predictor for development of TA.

Discussion

The main results of this study were that age, a history or presence of congestive heart failure, postoperative development of a systemic inflammatory response syndrome or sepsis, the severity of multiple organ dysfunction syndrome and in particular the severity of cardiovascular failure proved to be independent risk factors associated with development of tachyarrhythmias in cardiac surgery patients.

Age increased risk by approximately 12% per decade. This result is in line with previous reports (1, 2, 7, 8). Age has been shown to be strongly associated with development of atrial fibrillation in other types of surgery and also unrelated to surgery (9, 10). In this study atrial fibrillation and flutter were by far the most important TA, accounting for 75% of all episodes. Although the exact mechanisms of TA development in the elderly heart are not known, age-associated changes in the atria such as muscle atrophy, dilatation and increasing heterogeneity in electrical conduction have been suggested to explain this strong association (11). The influence of presence or history of congestive heart failure on subsequent TA development in surgical patients is much less clear (2, 12). However, a strong association between congestive heart failure and atrial fibrillation has been demonstrated in non-surgical patients in the Framingham Heart Study (10).

Although emergency procedures, surgery involving the mitral valve, combined valve and coronary artery surgery as well as prolonged bypass and aortic cross-clamp times were univariately associated with TA-development, neither factor proved to be independently associated with postoperative TA. One would expect time on cardiopulmonary bypass, and in particular aortic cross-clamp time, to be of importance in determining the extent of myocardial injury significantly affecting the threshold for postoperative arrhythmogenesis. Interestingly, other investigations have also failed to show that the duration of aortic cross-clamp time or cardiopulmonary bypass is a strong predictor of postoperative TA (1). Recently a significantly higher incidence of atrial fibrillation has been demonstrated for moderate hypothermic (28°C) when compared with mild hypothermic (34°C) cardiopulmonary bypass (13). Since in the present study all patients were intraoperatively managed with mild

hypothermic cardiopulmonary bypass, differences in myocardial protection due to changes in intraoperative management can be ruled out as factors influencing postoperative TA development.

It is well known that the degree of physiologic derangement during the first 24 h following admission to an ICU is correlated with morbidity and patient mortality. Higher admission SAPSc was univariately associated with subsequent TA development. Similarly Brathwaite and Weissman found significantly higher admission APACHE II-scores in patients undergoing major noncardiothoracic surgery who subsequently developed atrial arrhythmias when compared with control patients (14).

The most interesting result of this retrospective analysis was that development of clinical syndromes SIRS and sepsis and degree of multiple organ dysfunction syndrome were significant independent risk factors associated with TA. Myocardial dysfunction including decreases in right and left ventricular ejection fraction and left ventricular dilatation accompanying SIRS and sepsis have already been described by different authors (15–17). However, an association with cardiac tachyarrhythmias is less well established (18). Almost 20 years ago Ledingham and McArdle observed that development of atrial fibrillation is not unusual in patients with septic shock (19). In a study in patients undergoing major noncardiothoracic surgery and subsequently developing atrial arrhythmias, 15% died because of sepsis, while in a control group sepsis accounted only for 3% of patients' deaths (14). A recent investigation on TA in cardiac surgical patients described a significant association between postoperative acute phase response, assessed by measurements of serum CRP-concentrations, and subsequent development of TA (20). It is well known that cardiac surgery involving cardiopulmonary bypass technique may lead to gastrointestinal ischemia, increased mucosal permeability and subsequent endotoxemia promoting production and increased release of proinflammatory cytokines (21, 22). Interestingly, only a minority of patients develop SIRS. A recent investigation showed that pre-existence of high antibody concentrations against the core portion of endotoxin in cardiac surgery patients was associated with significantly reduced postoperative patient morbidity (23). One might speculate that similar factors may be of importance in the complex genesis of tachyarrhythmias after cardiac surgery.

Multiple organ dysfunction syndrome was significantly more severe in patients developing TA, increasing the relative risk by 1.37 per point increase in MODS-score. By introducing the degree of specific organ dysfunction into multivariate analysis only severity of cardiovascular failure was an independent predictor for development of TA. Since severity of cardiovascular failure is mainly assessed by the extent of catecholamine support, we speculate that catecholamine stress may have been of major importance in arrythmogenesis in these patients. It is well known that vasoactive and inotropic drugs may induce cardiac arrhythmias in a dose related manner. Morady and Halter found that in physiologic doses epinephrine shortens effective refractory period of the atrium, AV node and ventricle (24). It improves AV node conduction and may consequently facilitate the induction of sustained ventricular tachycardia. Culling and Penny observed that alpha-adrenoreceptor stimulation with methoxamine may induce ventricular tachycardia or fibrillation during ischemia or reperfusion (25). Phosphodiesterase-inhibitors have been reported to increase electrical conduction and to decrease refractory period within atria and atrio-ventricular node (26). A recent study in patients undergoing a dobutamine-stress test demonstrated significant TA, including ventricular tachycardia and atrial fibrillation at higher dosages of dobutamine, preferentially occurring in older patients and patients with significant myocardial ischemia (27).

During the study period the overall incidence of tachyarrhythmias was 15%. This number is in accordance with other investigations in cardiac surgery patients. Compared with an overall mortality rate of 2.7% in patients without TA, mortality increased 6-fold (16.8%) in TA patients. However, during the study period no patient died as a direct consequence of TA. TA were associated with a significant increase in ICU stay (8.6±9.2 days vs. 2.6±2.1 days) underlining previous reports demonstrating significantly increased total hospital costs in patients developing TA.

In conclusion, in cardiac surgery patients, age, a history or presence of congestive heart failure, postoperative development of a systemic inflammatory response syndrome or sepsis and the severity of multiple organ dysfunction syndrome are independent predictors for development of TA. Most striking was that the presence of SIRS and sepsis increased relative risk for TA 3.5-fold. The association of severity of cardiovascular dysfuntion with TA strongly points at a causal relationship between catecholamine therapy and TA development.

Appendix I

Definitions and grading of organ dysfunction (MODS-score) (modified from Goris et al. (5))

Function	*0*	*1*	*2*
Pulmonary	$PaO_2/FiO_2 \geq 300$	$PaO_2/FiO_2 \geq 250$	$PaO_2/FiO_2 < 250$
Renal	creatinine ≤2.0 mg%	creatinine > 2.0 mg%; doubling of creatinine in patients with previous compensated renal failure	acute hemofiltration
Hepatic	bilirubin <2.0 mg%; SGOT/SGPT within normal range	bilirubin 2–5 mg%; SGOT/SGPT ≤3 times normal value	bilirubin >5.0 mg%; SGOT/SGPT >3 times normal value
Hematologic	thrombocytes within normal range; normal coagulation	thrombocytes decrease ≥25%; abnormal PT/aPTT with and without bleeding	hemorrhagic diathesis; massive transfusion 5 blood products/h or >10 blood products/24 h
Cardiovascular	normal blood pressure; no vasoactive drugs except dopamine $\leq 5\ \mu g \cdot kg^{-1} \cdot min^{-1}$	fluid resuscitation >50% of normal need and/or dopamine $> 5\ \mu g\ kg^{-1} \cdot min^{-1}$, dobutamine $< 10\ \mu g \cdot kg^{-1} \cdot min^{-1}$, phenylephrine	dobutamine $> 10\ \mu g \cdot kg^{-1} \cdot min^{-1}$, epinephrine, norepinephrine, combination of catecholamines, IABP, VAD

PaO_2 – arterial oxygen tension; FiO_2 – fractional inspiratory oxygen concentration; SGOT – serum glutamic-oxaloacetic transaminase; SGPT – serum glutamic-pyruvic transaminase; IABP – intra-aortic balloon pump; VAD – ventricular assist device.

Appendix II

Definitions of SIRS and sepsis (6)

Systemic inflammatory response syndrome (SIRS): The systemic inflammatory response to a variety of severe clinical insults. The response is manifested by two or more of the following conditions:

Temperature >38°C or <36°C

Heart rate >90 beats/min

Respiratory rate >20 breaths/min or $PaCO_2$ <32 Torr (<4.3 kPa)

White blood cells >12 000 cells/mm^3, <4000 cells/mm^3, or >10% immature forms

Sepsis: The systemic response to infection. This systemic response is manifested by two or more of the following conditions as a result of infection:

Temperature >38°C or <36°C

Heart rate >90 beats/min

Respiratory rate >20 breaths/min or $PaCO_2$ <32 Torr (<4.3 kPa)

White blood cells >12 000 cells/mm^3, <4000 cells/mm^3, or >10% immature forms

Infection was suspected in patients with microbiological and/or radiological evidence for an infectious focus or in patients with bacteremia manifested by at least two positive blood cultures with the same microorganism obtained from different sites.

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