Incremental value of high-sensitive troponin T in addition to the revised cardiac index for peri-operative risk stratification in non-cardiac surgery

Michael Weber[1,2]*, Andreas Luchner[3], Seeberger Manfred[4], Christian Mueller[4], Christoph Liebetrau[1], Axel Schlitt[5], Svetlana Apostolovic[6], Radmilo Jankovic[6], Dragic Bankovic[7], Marina Jovic[7], Veselin Mitrovic[1], Holger Nef[1], Helge Mollmann[1], and Christian W. Hamm[1]

[1]Kerckhoff Heart and Thorax Center, Bad Nauheim, Germany; [2]Kreisklinik Groß-Umstadt, Krankenhausstrasse 11, 64823 Groß-Umstadt, Germany; [3]University of Regensburg, Regensburg, Germany; [4]University of Basel, Basel, Switzerland; [5]University of Halle, Halle, Germany; [6]Medical Center Nis, Nis, Serbia; and [7]University of Kragujevac, Kragujevac, Serbia

Aims	We aimed to evaluate the incremental value of high-sensitive troponin T (hsTnT) for risk prediction prior to non-cardiac surgery in comparison with the established revised cardiac index.
Methods and results	In this prospective, international multicentre observational study, 979 patients prior to non-cardiac surgery were enrolled. The endpoints were in-hospital mortality, the combination of death, acute myocardial infarction, cardiac arrest, cardio-pulmonary resuscitation, and acute decompensated heart failure. Twenty-five patients (2.6%) deceased and 36 (3.7%) of the patients experienced the combined endpoint. Cardiac markers were elevated in those patients who died when compared with survivors (hsTnT: 21 ng/L vs. 7 ng/L; $P < 0.001$; NT-proBNP: 576 pg/mL vs. 166 pg/mL; $P < 0.001$). Applying a cut-off for hsTnT of 14 ng/L and for NT-proBNP of 300 pg/mL, those patients with elevated hsTnT had a mortality of 6.9 vs. 1.2% ($P < 0.001$) and with elevated NT-proBNP 4.8 vs. 1.4% ($P = 0.002$). The highest AUC of the ROC curve was found for hsTnT as a predictor for mortality of 0.809. In a multivariate Cox regression analyses, hsTnT was the strongest independent predictor for the combined endpoint [HR 2.6 (95% CI: 1.3–5.3); $P = 0.01$].
Conclusion	High-sensitive troponin T provides strong prognostic information in patients undergoing non-cardiac surgery incremental to the widely accepted revised cardiac index.
Keywords	High-sensitive Troponin T • Cardiac risk • Non-cardiac surgery • NT-proBNP

Introduction

Non-cardiac surgical procedures are frequently performed in European countries. Approximately 1.5% of the population are undergoing major surgical procedures annually.[1]

However, surgical interventions are associated with relevant cardiovascular morbidity and mortality. Data on cardiac outcome can be derived from a few large-scale clinical trials and registries that have been undertaken in patients undergoing non-cardiac surgery with major complications rate varying from 1.7 to 3.5%.[2–5]

In most cases, non-cardiac surgery is performed as an elective intervention rendering sufficient time for peri-operative risk assessment. Currently, several clinical risk indices are applied. The most common ones are the cardiac risk index from Goldman et al., the modified risk index from Detsky et al. and most recently introduced the revised cardiac risk index from Lee et al.[6–8] Further tools for risk stratification have been provided by the ACC/AHA guidelines on peri-operative cardiovascular evaluation for non-cardiac surgery and by the American Society of Anaesthesiologists (ASA).[9]

Cardiac markers, namely troponins and B-type natriuretic peptides (BNPs), have been recognized as powerful biomarkers reflecting myocardial injury, respectively, myocardial stress as a consequence of a variety of underlying pathologies such as heart failure, coronary artery disease, and valvular heart disease. There is convincing evidence from a great number of studies that BNP and NT-proBNP provide strong prognostic information in patients across a broad spectrum of cardiovascular disorders as well as in apparently healthy individuals.[10,11]

Cardiac-specific troponins are the gold standard for the diagnosis of acute myocardial infarction for several years.[12] However more recently, with the introduction of the new high-sensitive troponin assays, there is growing evidence, that troponins are also elevated in patients with various cardiovascular diseases, such as heart failure or stable coronary heart disease, reflecting minor myocardial injury and thus providing prognostic information.[13,14]

Therefore, it was the aim of our study to evaluate the usefulness of cardiac troponin T (TnT) measured by a new high-sensitive troponin T assay (hsTnT) for risk stratification of patients undergoing non-cardiac surgery in comparison with an established clinical risk index and NT-proBNP.

Methods

Patients

The study was conducted as an international multicentre, observational study including patients undergoing major non-cardiac surgery. A total of 979 patients were recruited between 2006 and 2009 from eight hospitals located in Germany, Switzerland, Serbia, and Spain.

Inclusion criteria were major non-cardiac surgery (abdominal, urological, orthopaedic, gynaecologic, neck surgery, and vascular surgery) in general anaesthesia, an age >55 years and at least one of the following cardiovascular risk factors—diabetes mellitus, hypertension, hyperlipidaemia, active smoking, or a family history of cardiac disease. Exclusion criteria were emergent surgery and the disability to understand or to sign informed consent.

All the patients included into the study signed informed consent, which included biomarker analyses. The study has been approved by the local ethical boards of the participating centres.

Clinical endpoints

As primary endpoint all-cause mortality and the combination of all cause mortality, acute myocardial infarction, cardiac arrest or ventricular fibrillation, cardio-pulmonary resuscitation, and acute decompensated heart failure during hospitalisation were pre-defined. As secondary endpoints, total hospital stay and requirement of intensive care treatment were assessed. The first occurring event and the time until this event have been assessed. For the mortality analyses, only death and the time until death has been evaluated.

Endpoint assessment was carried out according to clinical standards of the respective centres. The diagnosis of peri- or post-operative myocardial infarction was made on the basis of the universal definition of myocardial infarction.[12] Briefly, an elevated troponin level with a rise and fall pattern together with clinical signs of myocardial ischaemia was considered as myocardial infarction.

Surgical procedures

Patients undergoing major non-cardiac surgery were included. Procedures had to be performed under general anaesthesia. Surgical procedures were performed according to clinical standards of the respective hospitals. A list of the different kinds of surgical procedures performed is presented in *Table 1*.

Revised cardiac index (Lee index)

We calculated the revised cardiac risk index (Lee index) as described in detail previously.[8] Briefly, one point was assigned to each of the following factors: a history of CAD, a history of cerebrovascular disease, heart failure, insulin-dependent diabetes mellitus, impaired renal function, and high-risk type of surgery.

Laboratory assessment

Blood samples were taken within 7 days prior to surgery. Samples were taken from an antecubital vein in tubes without additives and processed immediately. Serum was separated and frozen at $-70^{\circ}C$ until analyses. All analyses were performed after the end of the recruiting phase at the pre-defined core laboratories at the University of Basel and at the Kerckhoff Heart and Thorax Center in Bad Nauheim. The investigators at the different centres were blinded to the biomarker results.

Cardiac TnT was measured by a newly developed high-sensitive electrochemiluminescence-immunoassay (hsTnT) on an Elecsys analyzer (Roche Diagnostics, Mannheim, Germany). The lower limit of detection for this assay is 3 ng/L, the 99th percentile of a healthy reference population is 14 ng/L, and the concentration with a coefficient of variation (CV) <10% is 13 ng/L. NT-proBNP was measured by an electrochemiluminescence-immunoassay (Elecsys proBNP, Roche Diagnostics, Mannheim, Germany). The analytical range extends from 5 to 35 000 pg/mL. The total CV was 3.3% ($n = 28$) at a level of 252.6 pg/mL and 3.7% ($n = 25$) at a level of 6130.8 pg/mL of NT-proBNP.

Statistics

All results for continuous variables are expressed as means $\pm$ SD. Skewed variables are expressed as median and inter-quartile range. For group wise comparisons, the Mann−Whitney test (two-groups), the Kruskal−Wallis test (*n*-groups), Student's *t*-test (two-groups), or one-way ANOVA (*n*-groups) were used as appropriate. For categorical variables, Fisher's exact test or the χ^2 test were used. To evaluate test performance of NT-proBNP, hsTnT and the Lee index as predictors for mortality, respectively, the combined endpoint the area under the curve (AUC) of the receiver operating characteristics curve (ROC) has been calculated. Hazard ratios for all clinical variables were calculated by univariate Cox regression analyses. Multivariate Cox regression analysis was performed for the combined endpoint including the four strongest variables in the univariate analyses with $P <$ 0.1 in the univariate Cox regression analyses. All tests were performed two sided and a significance level of $P < 0.05$ was considered to indicate statistical significance. For all statistical analyses, the statistical software SPSS 10.0 (Statistical Package for the Social Sciences, Chicago, IL, USA) for Windows was used.

Results

Baseline characteristics of the patients are presented in *Table 1*. A total of 979 patients have been recruited, 46% females, mean age 69 years. A history of CAD, defined as prior bypass surgery, coronary intervention or myocardial infarction, was present in 25% of the patients. The majority of patients (57%) had two or more cardiovascular risk factors and 87% of the patients were under

Table 1 Baseline characteristics

	All patients	Survivors	Deceased	P-value survivors vs. deceased
n (%)	979	954 (97.4)	25 (2.6)	
Gender (female) n (%)	447 (46)	440 (46)	7 (28)	0.102
Age (years) AM $\pm$ SD	69 $\pm$ 8	69 $\pm$ 8	68 $\pm$ 9	0.788
BMI (kg/m^2) median (IQR)	27 (24−30)	27 (24−30)	27 (24−30)	0.493
CAD, n (%)	246 (25)	238 (25)	8 (32)	0.483
Dyspnoea (NYHA II−IV), n (%)	293 (30)	281 (30)	12 (48)	0.074
Angina pectoris (CCS II−III) n (%)	106 (11)	99 (10)	7 (28)	0.013
Atrial fibrillation, n (%)	74 (7.6)	71 (7.4)	3 (12)	0.927
Diabetes mellitus, n (%)	258 (27)	251 (26)	7 (28)	0.821
Insulin dependent, n (%)	77 (7.9)	74 (7.7)	3 (12)	0.716
Hypertension, n (%)	860 (88)	843 (88)	18 (72)	0.023
Hyperlipidaemia, n (%)	334 (34)	328 (34)	6 (24)	0.548
Active smoker, n (%)	250 (26)	242 (25)	8 (32)	0.486
Aspirin/clopidogrel, n (%)	435 (44)	421 (44)	14 (56)	0.308
Beta-blocker, n (%)	472 (48)	462 (48)	10 (40)	0.426
ACE inhibitor/AT-antagonist, n (%)	582 (59)	569 (60)	13 (52)	0.537
Diuretics, n (%)	303 (31)	293 (31)	10 (40)	0.380
Nitrates, n (%)	98 (10)	91 (9.5)	7 (28)	0.009
Anticoagulation, n (%)	89 (9)	83 (9)	6 (24)	0.02
Lee index				
0 n (%)	277 (28)	275 (29)	2 (8)	0.010
1 n (%)	450 (46)	439 (46)	11 (44)	
2 n (%)	187 (19)	178 (19)	9 (36)	
$\geq$3 n (%)	65 (7)	62 (7)	3 (12)	
Hb (g/dL) median (IQR)	13.6 (12.4−14.7)	13.6 (12.5−14.7)	13.1 (11.7−14.7	0.268
Creatinine (mg/dL) median (IQR)	0.9 (0.76−1.1)	0.90 (0.76−1.1)	0.97 (0.81−1.2)	0.299
hs-TNT (ng/L) median (IQR)	7 (3−14)	7 (3−13)	21 (12−33)	<0.001
NT-proBNP (pg/mL) median (IQR)	171 (79−439)	166 (77−428)	576 (271−2119)	<0.001
hsTnT >14 ng/L, n (%)	233 (24)	217 (23)	16 (64)	<0.001
NT-proBNP >300 pg/mL, n (%)	335 (34)	319 (33)	16 (64)	0.002

n, numbers; IQR, inter-quartile range; BMI, body mass index; CAD, coronary artery disease.
Baseline data of the patients according to survival status.

cardiovascular medical treatment. A Lee index of 0 was present in 277 (28%), of 1 in 450 (46%), of 2 in 187 (19%), and $\geq$3 in 65 (7%) patients.

Patients were hospitalized for a median period of 11 (IQR: 7−17) days. During this period 25 (2.6%) patients died and 36 (3.7%) patients experienced the combined endpoint (1 patient with acute myocardial infarction, 4 patients with ventricular fibrillation, 12 patients requiring CPR, 9 patients with acute decompensated heart failure, and 10 patients died without any preceding endpoint).

Patients who deceased had more frequently pre-existing angina pectoris, a history of arterial hypertension, a pre-medication of nitrates or oral anticoagulation, a higher Lee index, hsTnT >14 ng/L, and NT-proBNP $\geq$300 pg/mL.

The type of surgery and the mortality rates are presented in Table 2. More than half of the patients underwent either vascular or abdominal surgery.

Table 2 Type of surgery and mortality

	n (%)	Deaths n (%)		
		Total	hsTnT >14 ng/L (%)	hsTnT $\leq$14 ng/L (%)
Abdominal	254 (26)	10 (3.9)	7/50 (14.0)	3/204 (1.5)
Vascular surgery	252 (26)	7 (2.8)	4/81 (4.9)	3/171 (1.8)
Orthopedy/ trauma	77 (8)	1 (1.3)	1/23 (4.3)	0/54 (0)
Gynaecology	110 (11)	1 (0.9)	1/9 (11.1)	0/101 (0)
Others	286 (29)	6 (2.1)	3/70 (4.3)	3/216 (1.4)

Distribution of the different types of surgery performed on the patients included into the study and mortality rates.

High-sensitive troponin T values according to comorbidities are depicted in *Table 3*.

For the entire population, NT-proBNP was at median 171 pg/mL (IQR: 79–439) and hsTnT was 7 ng/L (IQR 3–14). Both markers were higher in those patients who died during hospitalization when compared with those who survived [NT-proBNP 576 (271–2119) vs. 166 (77–428) pg/mL; $P < 0.001$ and hsTnT 21 (12–33) vs. 7 (3–13) ng/L; $P < 0.001$]. In the entire cohort, 335 (34%) patients had a NT-proBNP serum concentration >300 pg/mL and 233 (24%) patients had hsTnT $\geq$ 14 ng/L. The occurrence of the combined endpoint was strongly related to elevated NT-proBNP ($\geq$ 300 pg/mL), elevated hsTnT (>14 ng/L), and the Lee index (*Figure 1A*). Comparable results could be observed for in-hospital mortality (*Figure 1B*).

The ROC curves of hsTnT, NT-proBNP, and the Lee index as predictors for the combined endpoint and for in-hospital mortality showed a significant AUC for all parameters, with the highest AUC for hsTnT of 0.784 for the prediction of the combined endpoint and of 0.809 for the prediction of in-hospital mortality. Comparing the AUC of Lee index, hsTnT, and NT-proBNP, we found no difference between NT-proBNP and the Lee index but a significant higher AUC of hsTnT compared with the Lee index for the prediction of mortality. However, for the combined endpoint, the AUC for hsTnT was larger but this difference did miss statistical significance. (*Figure 2A* and *B*).

Table 3 High-sensitive troponin T values according to comorbidities

	hsTnT (ng/L)		
	Median	IQR	*P*-value
Creatinine >1.2 mg/dL			
Yes	16	8–33	<0.001
No	6	3–12	
History of CAD			
Yes	11	5–20	<0.001
No	6	3–12	
Diabetes mellitus			
Yes	8	4–17	0.002
No	7	3–13	
Active smoker			
Yes	7	3–14	0.698
No	7	3–13	
Hypertension			
Yes	7	3–14	0.218
No	6	3–15	
Age >65 years			
Yes	9	4–17	<0.001
No	3	3–8	
Obese (BMI >27)			
Yes	6	3–12	<0.001
No	8	3–16	

Values of high-sensitive troponin T according to various comorbidities.

Univariate Cox regression analysis revealed that the Lee index as well as NT-proBNP and hsTnT were significantly associated with an increased risk for the combined endpoint and for in-hospital mortality if entered as dichotomized variable (*Table 4*).

In a multivariate Cox regression analysis, hsTnT >14 ng/L was the strongest independent predictor for the combined endpoint as well as for in-hospital mortality. In contrast, NT-proBNP and the Lee index lost its value as an independent risk predictor (*Table 5*).

HsTnT >14 ng/L was significantly associated with a higher event rate in each risk category according to the Lee index (*Figure 3A* and *B*).

The length of hospital stay was significantly longer in those patients with a higher Lee index (8 vs. 11 vs. 13 days; $P < 0.001$) and in patients with elevated hsTnT (10 vs. 12 days; $P < 0.001$). Intensive care treatment post-operatively was necessary in 351 patients (36%). The number of patients requiring intensive care treatment was higher in patients with elevated NT-proBNP, with elevated hsTnT, and was related to the Lee index (*Figure 4*).

Discussion

In the present study, we aimed to analyse the additive value of the cardiac marker hsTnT in addition to the revised cardiac index (Lee index) and NT-proBNP to identify patients at a high risk for adverse cardiac events undergoing major non-cardiac surgery.

The key finding is that both cardiac markers provide predictive information for the occurrence of serious clinical events, which is incremental to that obtained by the established and most widely applied clinical risk score, the revised cardiac risk index.[8] However, hsTnT was the strongest independent risk predictor. Furthermore, we found that pre-operative levels of both cardiac markers were associated to the length of hospital stay and the necessity of intensive care treatment.

Pre-operative risk assessment is of great clinical importance. In most cases non-cardiac surgery is performed as an elective procedure allowing thorough investigation of the patient and accurate risk evaluation in order to indicate a surgical procedure. Several situations need to be distinguished. First, a patient undergoes non-cardiac surgery for a prognostic indication. In this scenario, the benefit of surgery and the associated risk need to be counterbalanced. Secondly, a patient undergoes non-cardiac surgery for a symptomatic indication. In this situation, the patient needs to be informed about his individual risk of the procedure to be able to sign an informed consent. Thirdly, a patient unavoidably requires surgery for a vital indication. In this case, risk assessment is of minor interest. However, in high-risk patients the question might arise in how far the cardiac risk can be attenuated by specific means. Therefore, in all cases precise risk stratification is essential.

Within the last decades, several risk indices based on observational data have been introduced. Currently, the most widely accepted risk index for patients undergoing non-cardiac surgery is the revised cardiac risk index.[8] It has been developed from prospectively collected data from a total of 4315 patients divided into a derivation and a validation cohort. The Lee index can be calculated from six clinical and easily achievable variables providing a score from 0 to 6 points. In the original description, the incidence
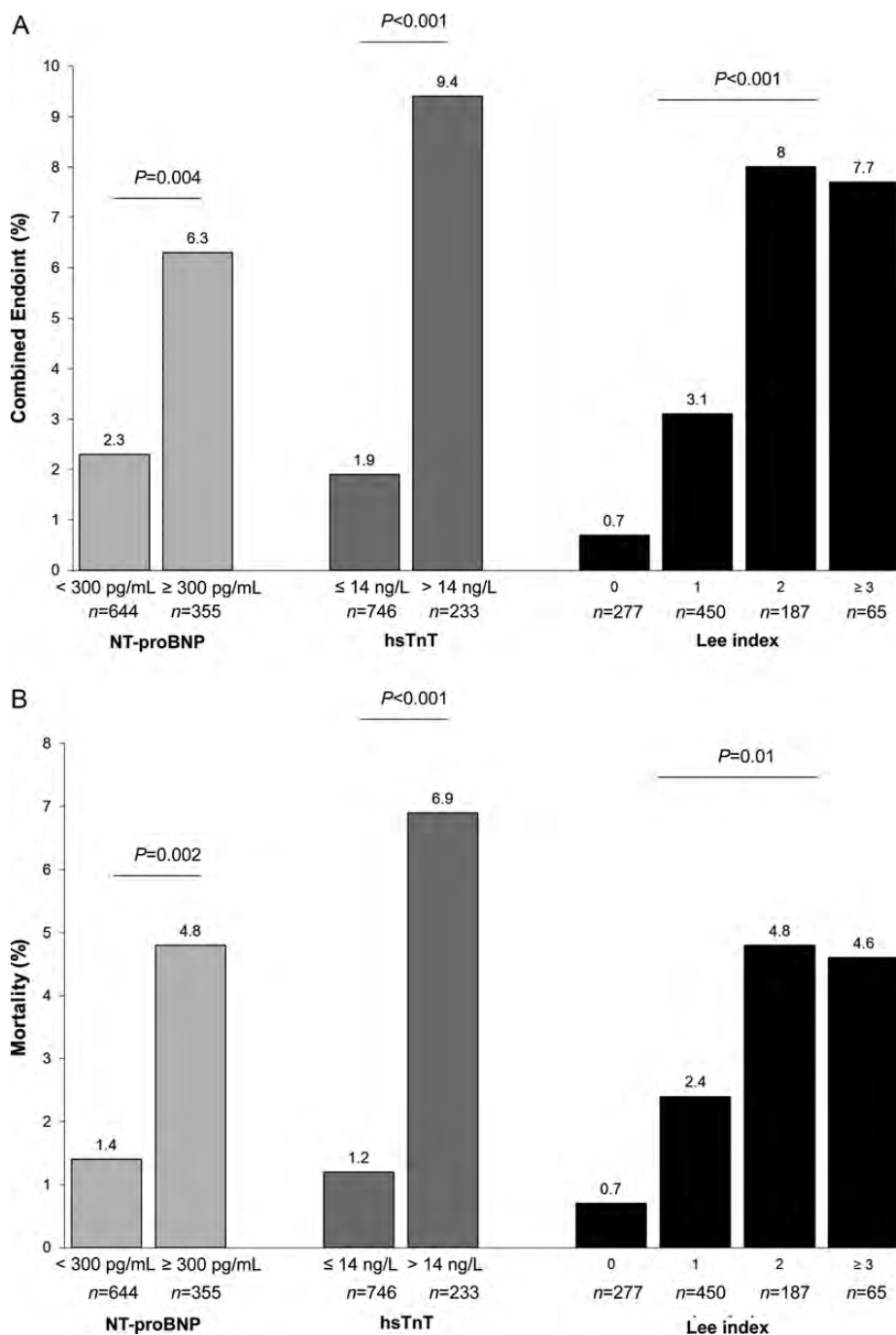
Figure 1 The frequency of the combined endpoint (A) and in-hospital mortality (B) in association to NT-proBNP (light grey bars), hsTnT (grey bars), and the revised cardiac index 'Lee index' (dark grey bars).

of major cardiac complications has been reported as being strongly associated to the revised Lee index both, in the derivation and in the validation cohort. In our study, which included a comparable subset of patients, we also found a strong and stepwise association of adverse cardiac events to the revised cardiac index, confirming these previous data.

Several studies published within the last years have demonstrated a prognostic value of pre-operative BNPs levels for cardiac events in patients undergoing non-cardiac surgery.[15,16] In all of these studies, BNP or NT-proBNP was independently associated with an increased risk. Whereas all the studies adjusted for a variety of clinical factors, only in one of the studies the revised cardiac index was included in the multivariate analysis. In three other studies, either the Goldmann index or the ASA score has been added to the analyses. Our data further confirm these previous data demonstrating a significant association between
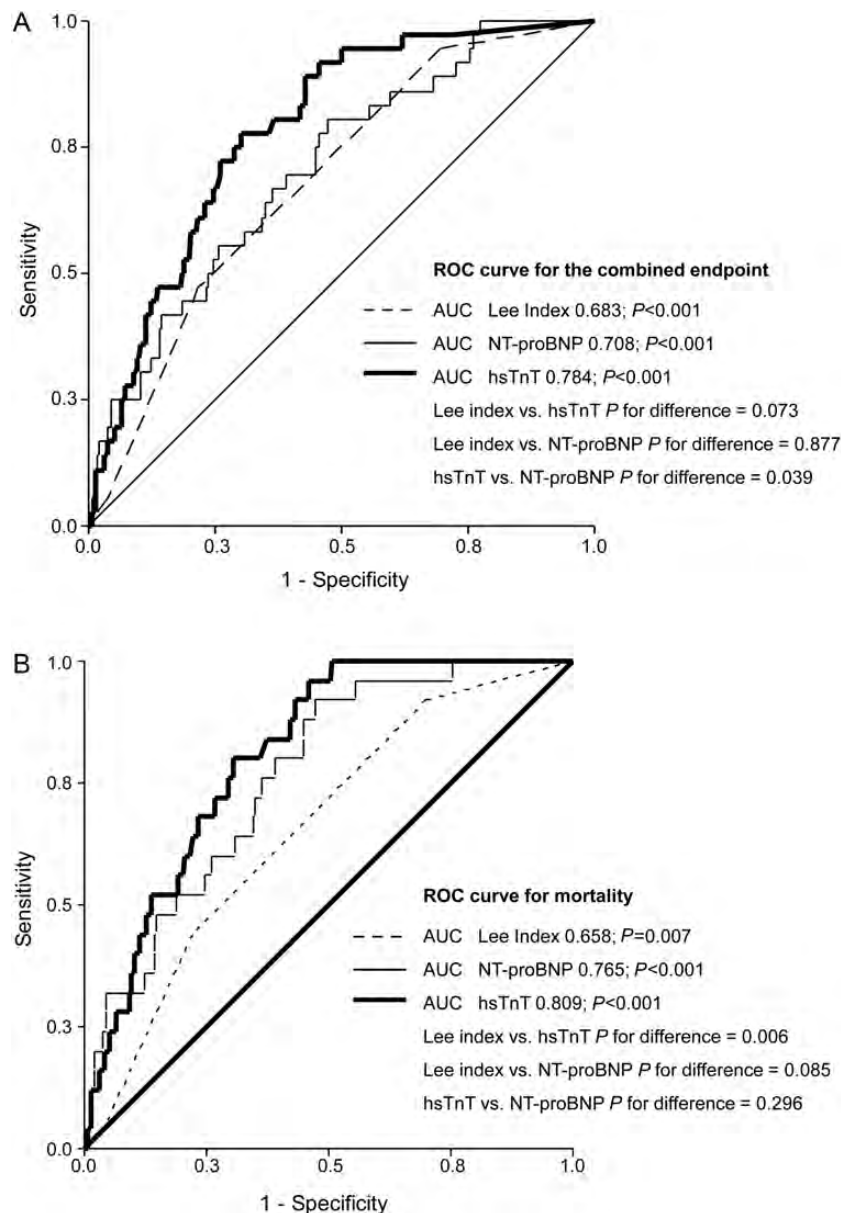
Figure 2 ROC curves of NT-proBNP, hsTnT, and the revised cardiac index 'Lee index' for the combined endpoint (*A*) and in-hospital mortality (*B*).

NT-proBNP and peri- and post-operative cardiac events which was incremental to the revised cardiac index.

However, in none of those previously published studies, a comparative analysis with pre-operative troponin assessment has been performed. In fact, there are no available data evaluating pre-operative troponin testing as a predictor for post-operative cardiac events in non-cardiac surgery. There are only data available from three smaller studies which evaluated the value of post-operative troponin testing, consistently demonstrating that patients with elevated troponin after non-cardiac surgery were at a higher risk for subsequent cardiac events.[17,18]

With the introduction of a new generation of high-sensitive assays, much lower troponin concentrations are detectable with sufficient analytical precision. With those assays, troponins are measurable also in apparently healthy individuals. Furthermore, low-level elevation of troponins is detectable in patients with cardiovascular diseases other than acute coronary syndromes, providing strong prognostic information.[13,14,19,20] Thus, the detection of low-level troponin elevation, which is indicative for minor myocardial damage, in apparently stable patients and non-acute subjects suggests a potential new indication of troponins as a risk indicator in other clinical scenarios besides acute coronary syndromes.

Table 4 Univariate Cox regression analyses

	B	Wald	P-value	HR	95% CI	
					Lower	Upper
hsTnT >14 ng/L	1.32	14.66	0.0001	3.73	1.90	7.31
Lee score ≥2	1.04	9.65	0.0019	2.84	1.47	5.48
NYHA class II−V	0.85	6.44	0.0112	2.35	1.21	4.53
Systolic blood pressure (mmHg)	−0.02	5.73	0.0166	0.98	0.97	1.00
Heart rate (/min)	0.03	5.60	0.0180	1.03	1.00	1.05
Pre-existing coronary artery disease	0.78	5.33	0.0210	2.17	1.12	4.20
Pre-treatment with ASS or clopidogrel	0.76	4.73	0.0297	2.13	1.08	4.23
NT-proBNP >300 pg/mL	0.72	4.47	0.0345	2.05	1.05	3.99
Angina pectoris CCS II−IV	0.67	2.96	0.0851	1.94	0.91	4.15

Univariate Cox regression analyses of various variables as a predictor for the combined endpoint of mortality, acute myocardial infarction, cardiac arrest or ventricular fibrillation, cardio-pulmonary resuscitation, and acute decompensated heart failure. Depicted are all variables with a P-value <0.1.

Table 5 Multivariate Cox regression analyses

	B	Wald	P-value	HR	95% CI	
					Lower	Upper
hsTnT >14 ng/L	0.96	6.86	0.0088	2.60	1.27	5.31
Lee score ≥2	0.64	3.04	0.0812	1.89	0.92	3.88
Systolic blood pressure (mmHg)	−0.01	1.41	0.2347	0.99	0.98	1.01
NYHA class II−IV	0.62	3.12	0.0774	1.87	0.93	3.73

Multivariate Cox regression analyses for the combined endpoint of mortality, acute myocardial infarction, cardiac arrest or ventricular fibrillation, cardio-pulmonary resuscitation, and acute decompensated heart failure adjusted for the four strongest variables with $P < 0.1$ in the univariate analyses.

In our study, we were able to evaluate pre-operative assessment of hsTnT as a risk indicator for subsequent adverse cardiac events in a cohort of stable patients undergoing non-cardiac surgery. Applying a cut-off value of 14 ng/L which is equivalent to the 99th percentile of a healthy population and which is recommended for the diagnosis of myocardial infarction according to the universal definition of myocardial infarction, we found elevated levels in one-fourth (24%) of the entire cohort. However, in those patients who died, elevated levels were found in two-thirds (64%) of the patients. Pre-operatively hsTnT levels elevated above this cut-off were associated with a 2.6-fold increase in in-hospital mortality, acute myocardial infarction, cardiac arrest or ventricular fibrillation, cardio-pulmonary resuscitation, and acute decompensated heart failure, and proved to be the strongest predictor, superior to the revised cardiac index and to NT-proBNP, for an adverse outcome after non-cardiac surgery. Therefore, hsTnT was the best parameter to identify a subset of individuals at extremely high risk for peri- or post-operative adverse cardiac events. The clinical implications, however, are uncertain. We might speculate that applying hsTnT to risk stratification, we will be able to identify those patients who are at a high risk and who benefit from risk reduction strategies. This hypothesis, however, needs to be tested in prospective interventional studies.

This study has several limitations with respect to the endpoint assessment. We did not have an independent endpoint committee which adjudicated the respective endpoints. However, since the most frequent endpoint was all-cause mortality and the results for the single endpoint all-cause mortality and the combined endpoint were very similar, the risk of a systematic error is negligible, especially since all investigators were blinded to biomarker results. Because of the study design the results are applicable only to patients undergoing non-cardiac surgery with at least one cardiovascular risk factor and may not be generalizable to subjects without any cardiovascular risk factor undergoing non-cardiac surgery. We might have missed some myocardial infarctions since we did not perform assessment of cardiac markers postoperatively. Since the results of NT-proBNP and hsTnT were not available for the investigators, a systematic bias is most unlikely.

In the current guidelines of the ESC on pre-operative cardiac risk assessment, it is outlined that risk reduction strategies, including pharmacological interventions or non-invasive imaging, should be reserved for patients with high risk. Furthermore, the application of the Lee index for cardiac risk stratification receives a class I A recommendation in these guidelines. In the present study, we were able to demonstrate that adding hsTnT assessment to the Lee index, peri-operative risk stratification can be improved substantially. Therefore, it can be speculated that hsTnT is highly
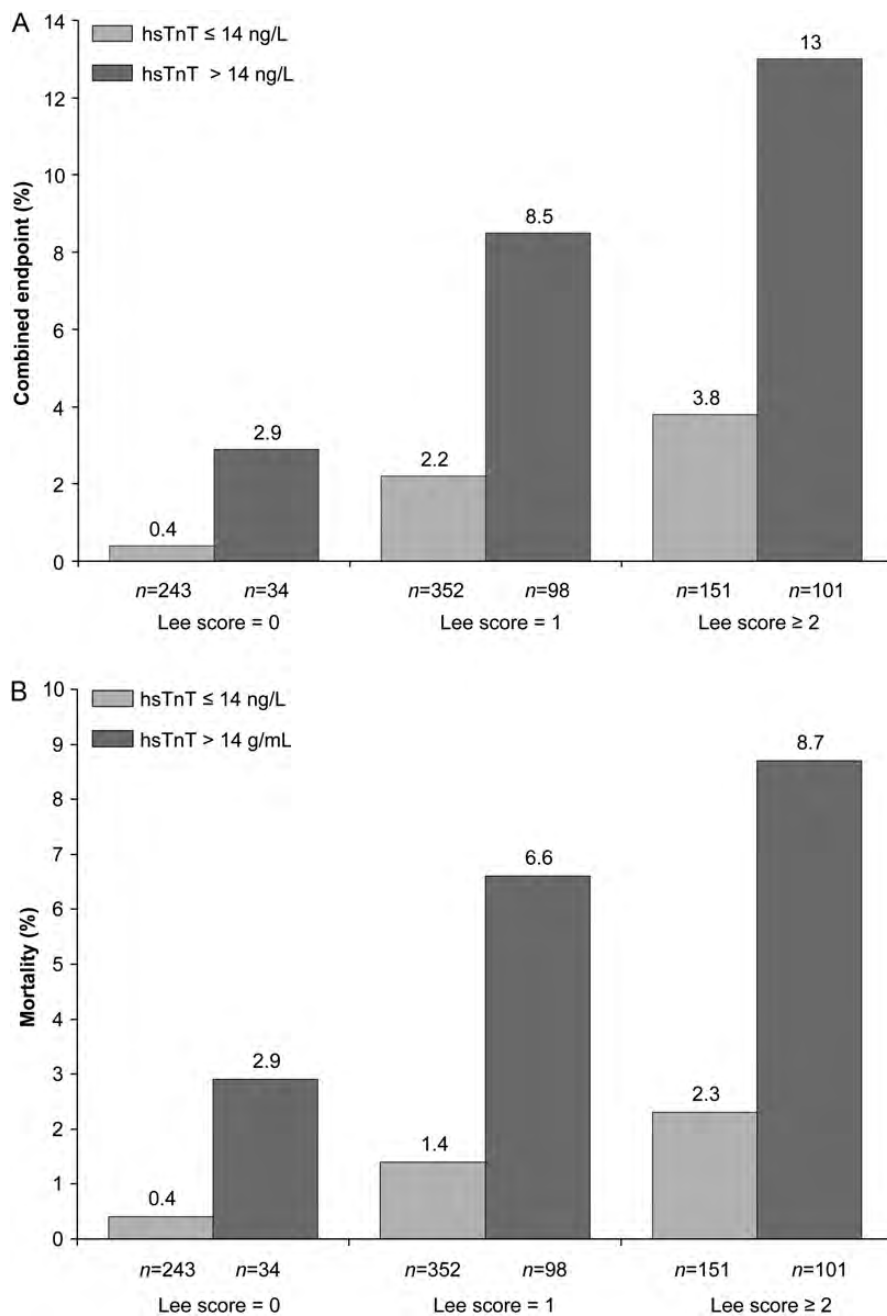
Figure 3 The frequency of the combined endpoint (*A*) and in-hospital mortality (*B*) in association hsTnT levels and the revised cardiac index 'Lee index'.

valuable to assign patients to an appropriate and individualized risk reduction strategy more accurately. However, these preliminary data need to be confirmed in further studies.

Conclusion

In the present study, we were able to demonstrate that the assessment of hsTnT adds incremental prognostic information to the established revised cardiac index (Lee index) and NT-proBNP. The assessment of hsTnT in addition to the revised cardiac index and NT-proBNP prior to non-cardiac surgery denotes an easily attainable method to achieve improved pre-operative risk stratification.
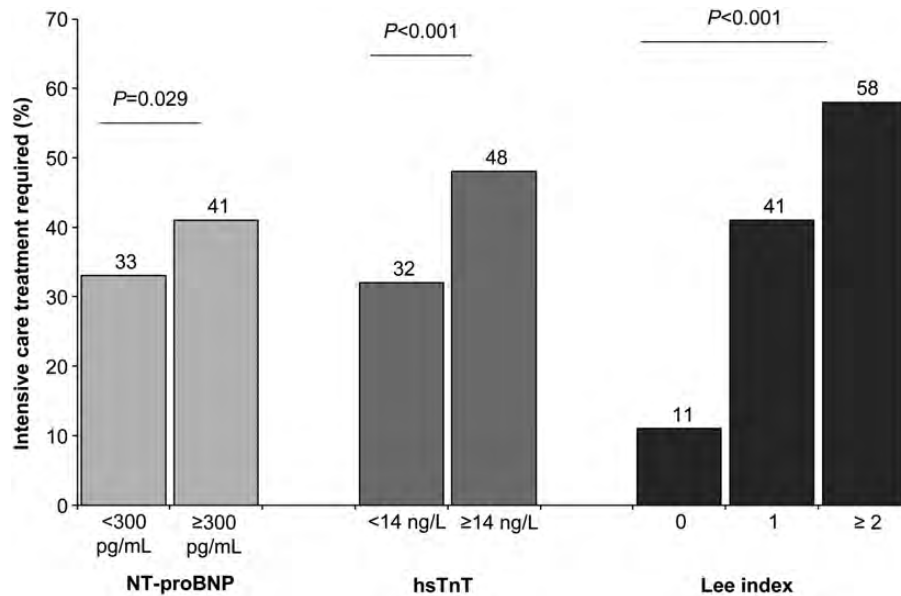
Acknowledgments

Figure 4 The frequency of the necessity of intensive care treatment to NT-proBNP (light grey bars), hsTnT (grey bars), and the revised cardiac index 'Lee index' (dark grey bars).

Funding

References

1. Poldermans D, Bax JJ, Boersma E, De Hert S, Eeckhout E, Fowkes G, Gorenek B, Hennerici MG, Iung B, Kelm M, Kjeldsen KP, Kristensen SD, Lopez-Sendon J, Pelosi P, Philippe F, Pierard L, Ponikowski P, Schmid JP, Sellevold OF, Sicari R, Van den Berghe G, Vermassen F. Guidelines for pre-operative cardiac risk assessment and perioperative cardiac management in non-cardiac surgery. *Eur Heart J* 2009;**30**:2769–2812.

2. Boersma E, Kertai MD, Schouten O, Bax JJ, Noordzij P, Steyerberg EW, Schinkel AF, van Santen M, Simoons ML, Thomson IR, Klein J, van Urk H, Poldermans D. Perioperative cardiovascular mortality in noncardiac surgery: validation of the Lee cardiac risk index. *Am J Med* 2005;**118**:1134–1141.

3. Poldermans D, Bax JJ, Kertai MD, Krenning B, Westerhout CM, Schinkel AF, Thomson IR, Lansberg PJ, Fleisher LA, Klein J, van Urk H, Roelandt JR, Boersma E. Statins are associated with a reduced incidence of perioperative mortality in patients undergoing major noncardiac vascular surgery. *Circulation* 2003;**107**:1848–1851.

4. Poldermans D, Bax JJ, Schouten O, Neskovic AN, Paelinck B, Rocci G, van Dortmont L, Durazzo AE, van de Ven LL, van Sambeek MR, Kertai MD, Boersma E. Should major vascular surgery be delayed because of preoperative cardiac testing in intermediate-risk patients receiving beta-blocker therapy with tight heart rate control?. *J Am Coll Cardiol* 2006;**48**:964–969.

5. Poldermans D, Boersma E, Bax JJ, Thomson IR, van de Ven LL, Blankensteijn JD, Baars HF, Yo TI, Trocino G, Vigna C, Roelandt JR, van Urk H. The effect of bisoprolol on perioperative mortality and myocardial infarction in high-risk patients undergoing vascular surgery. Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group. *N Engl J Med* 1999;**341**:1789–1794.

6. Detsky AS, Abrams HB, McLaughlin JR, Drucker DJ, Sasson Z, Johnston N, Scott JG, Forbath N, Hilliard JR. Predicting cardiac complications in patients undergoing non-cardiac surgery. *J Gen Intern Med* 1986;**1**:211–219.

7. Goldman L, Caldera DL, Nussbaum SR, Southwick FS, Krogstad D, Murray B, Burke DS, O'Malley TA, Goroll AH, Caplan CH, Nolan J, Carabello B, Slater EE. Multifactorial index of cardiac risk in noncardiac surgical procedures. *N Engl J Med* 1977;**297**:845–850.

8. Lee TH, Marcantonio ER, Mangione CM, Thomas EJ, Polanczyk CA, Cook EF, Sugarbaker DJ, Donaldson MC, Poss R, Ho KK, Ludwig LE, Pedan A, Goldman L. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation* 1999;**100**:1043–1049.

9. Fleisher LA, Beckman JA, Brown KA, Calkins H, Chaikof EL, Fleischmann KE, Freeman WK, Froehlich JB, Kasper EK, Kersten JR, Riegel B, Robb JF, Smith SC Jr, Jacobs AK, Adams CD, Anderson JL, Antman EM, Buller CE, Creager MA, Ettinger SM, Faxon DP, Fuster V, Halperin JL, Hiratzka LF, Hunt SA, Lytle BW, Nishimura R, Ornato JP, Page RL, Tarkington LG, Yancy CW. ACC/AHA 2007 Guidelines on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery) Developed in Collaboration With the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, and Society for Vascular Surgery. *J Am Coll Cardiol* 2007;**50**:1707–1732.

10. Thygesen K, Mair J, Mueller C, Huber K, Weber M, Plebani M, Hasin Y, Biasucci LM, Giannitsis E, Lindahl B, Koenig W, Tubaro M, Collinson P, Katus H, Galvani M, Venge P, Alpert JS, Hamm C, Jaffe AS. Recommendations for the use of natriuretic peptides in acute cardiac care: a position statement from the Study Group on Biomarkers in Cardiology of the ESC Working Group on Acute Cardiac Care. *Eur Heart J* 2012;**33**:2001–2006.

11. Weber M, Hamm C. Role of B-type natriuretic peptide (BNP) and NT-proBNP in clinical routine. *Heart* 2006;**92**:843–849.

12. Thygesen K, Alpert JS, White HD. Universal definition of myocardial infarction. *Eur Heart J* 2007;**28**:2525–2538.

13. Latini R, Masson S, Anand IS, Missov E, Carlson M, Vago T, Angelici L, Barlera S, Parrinello G, Maggioni AP, Tognoni G, Cohn JN. Prognostic value of very low plasma concentrations of troponin T in patients with stable chronic heart failure. *Circulation* 2007;**116**:1242–1249.

14. Omland T, de Lemos JA, Sabatine MS, Christophi CA, Rice MM, Jablonski KA, Tjora S, Domanski MJ, Gersh BJ, Rouleau JL, Pfeffer MA, Braunwald E. A sensitive cardiac troponin T assay in stable coronary artery disease. *N Engl J Med* 2009;**361**:2538–2547.

15. Dernellis J, Panaretou M. Assessment of cardiac risk before non-cardiac surgery: brain natriuretic peptide in 1590 patients. *Heart* 2006;**92**:1645–1650.

16. Karthikeyan G, Moncur RA, Levine O, Heels-Ansdell D, Chan MT, Alonso-Coello P, Yusuf S, Sessler D, Villar JC, Berwanger O, McQueen M, Mathew A, Hill S, Gibson S, Berry C, Yeh HM, Devereaux PJ. Is a pre-operative brain natriuretic peptide or N-terminal pro-B-type natriuretic peptide

measurement an independent predictor of adverse cardiovascular outcomes within 30 days of noncardiac surgery? A systematic review and meta-analysis of observational studies. *J Am Coll Cardiol* 2009;**54**:1599–1606.

17. Ausset S, Auroy Y, Lambert E, Vest P, Plotton C, Rigal S, Lenoir B, Benhamou D. Cardiac troponin I release after hip surgery correlates with poor long-term cardiac outcome. *Eur J Anaesthesiol* 2008;**25**:158–164.

18. Oscarsson A, Eintrei C, Anskar S, Engdahl O, Fagerstrom L, Blomqvist P, Fredriksson M, Swahn E. Troponin T-values provide long-term prognosis in elderly patients undergoing non-cardiac surgery. *Acta Anaesthesiol Scand* 2004; **48**:1071–1079.

19. de Lemos JA, Drazner MH, Omland T, Ayers CR, Khera A, Rohatgi A, Hashim I, Berry JD, Das SR, Morrow DA, McGuire DK. Association of troponin T detected with a highly sensitive assay and cardiac structure and mortality risk in the general population. *JAMA* 2010;**304**:2503–2512.

20. Hsieh BP, Rogers AM, Na B, Wu AH, Schiller NB, Whooley MA. Prevalence and prognostic significance of incidental cardiac troponin T elevation in ambulatory patients with stable coronary artery disease: data from the Heart and Soul study. *Am Heart J* 2009;**158**:673–679.

CARDIOVASCULAR FLASHLIGHT

Purulent pericarditis caused by a bad tooth

Qingbao Li[1†], Jie Zi[1†], Fang Liu[2,3†], and Decai Li[1]*

[1]Department of Cardiac Surgery, Provincial Hospital Affiliated to Shandong University, 324, Jingwu Road, Jinan 250021, China; [2]Department of Radiation Oncology, Qilu Hospital of Shandong University, 107, West Wenhua Road, Jinan 250012, China; and [3]Department of Image, Shandong Medical College, 5460, Erhuan Nanlu, Jinan 250002, China

* Corresponding author. Tel: +86 531 68776353, Email: dcaili@sina.com
[†] The authors contribute equally to this work.

A 14-year-old male was admitted for chest distress. Eight days ago, he picked his decayed tooth and experienced bleeding (*Panel A*, the arrow points to the bad tooth). An expansile submaxillary mass, diagnosed as cellulitis, appeared in 2 days (*Panel B*, CT showing the mass). Antibiotics were started and operative drainage was adopted (*Panel C*). But there was little improvement in the patient's condition and he began feeling chest distress. An echocardiogram showed much fluid in the pericardial cavity (*Panel D*). Ultrasound-guided percutaneous centesis was performed, and 1000 mL of pericardial pus was drained. The pus was sent for testing. *Streptococcus anginosus* was cultured, which was sensitive to vancomycin. Three days after vancomycin treatment, the amount of drained liquid decreased significantly. But another echocardiogram showed that there was still much pericardial pus. Another centesis was done, but unfortunately, the drainage tube lacerated the heart (*Panel E*, the right and left arrow points to the first and second drainage tube, respectively; *Panel F*, CT showing the thickened pericardium and drainage tubes).

During operation, lots of pus effused from communicated pretracheal space and retrosternal space. After the dropsical and thickened pericardium was cut open, considerable purulent secretion mixed with cellulose exudation was seen attached to the external surface of the heart (*Panel G*). The pus was cleared carefully, and most of the pericardium was cut off to release the heart. After the drainage tube, which pricked into the right ventricle, was pulled out, the injured heart was sutured. The pericardial cavity was washed with iodophors and normal saline at the end (*Panel H*). The patient tolerated the procedure well and was discharged after another 2 weeks of treatment with vancomycin. The occurrence of pericarditis owing to teeth problems is very rare. Moreover, purulent pericarditis caused by *Streptococcus anginosus* is also a rare.

Panels A–H. LV, left ventricle; RV, right ventricle; PS, pericardial space.