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Low molecular weight heparin in surgical valve procedures: When and how much for an optimal prophylaxis?

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Abstract

Background: *Periprocedural antithrombotic prophylaxis in patients undergoing surgical valve procedures (SVP) is insufficiently investigated. Low molecular weight heparin (LMWH) has been considered as an alternative to unfractionated heparin (UFH). However, safety and efficacy of this prophylaxis strategy is unknown. This study aimed to investigate safety and efficacy of periprocedural LMWH prophylaxis and determine optimal dosage and timing for periprocedural cessation and initiation.*

Methods: *The present study is a retrospective, single-center observational analysis of 388 patients who underwent SVP (valve replacement or valvuloplasty) between 2015 and 2016. In-hospital endpoints were bleeding, transfusions, reoperation due to bleeding, and thromboembolic events.*

Results: *Giving the first dose of LMWH on the day of SVP was a risk factor for bleeding (OR 1.07; 95% CI 1.04–1.10; $p < 0.001$), transfusions (OR 1.04; 95% CI 1.01–1.07; $p = 0.008$) and reoperation due to bleeding (OR 1.20; 95% CI 1.12–1.28; $p < 0.001$), with > 40 mg/day as a predictor. A higher dosage of LMWH premedication was an independent risk factor for bleeding (OR 1.02; 95% CI 1.00–1.04; $p = 0.03$) and transfusion (OR 1.03; 95% CI 1.01–1.05; $p = 0.01$), with > 60 mg/day as a predictor for these events. LMWH dosed within 24 h prior to SVP increased the risk of transfusion (AUC 0.636; 95% CI 0.496–0.762; $p = 0.04$).*

Conclusions: *Bleeding is an important early concern after surgical valve procedures. Safety and efficacy of periprocedural prophylaxis with LMWH depends on dosage and the timing of its administration. The most optimal periprocedural prophylaxis in the SVP population appears to be LMWH in dosage of 40–60 mg/day, which is recommended for deep vein thrombosis prophylaxis, ceased at least one day before SVP.* (Cardiol J XXXX; XX, X: xx–xx)

Key words: surgical valve procedure, bleeding complications, antithrombotic prophylaxis

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Introduction

Thromboembolic and bleeding events account for nearly three-quarters of early complications after surgical valve replacement (SVR) [1]. The risk of thromboembolic events is the highest in the first days after the procedure, reaching 4–8 cases per 100 patient-years [1–8]. However, the most common and life-threatening complication within the first 72 h after SVR is bleeding [1, 2, 9–12], which results from procedure-related coagulopathy caused by excessive consumption of plasma coagulation factors, enhanced platelet and fibrinolytic pathways activation during cardiopulmonary bypass (CPB), as well as a prolongation of coagulation cascade related to hypothermia [1, 13]. The risk of bleeding is further increased by the need for anticoagulation with unfractionated heparin (UFH) during SVR, reversal of its action with protamine sulfate, and its recirculation within 24 h after SVR [14, 15]. Although the early postprocedural period is burdened with a high risk of bleeding, antithrombotic prophylaxis is nevertheless required at the onset of SVR to avoid prosthesis thrombosis. There is a paucity of evidence guiding optimal antithrombotic prophylaxis after SVR and current recommendations are inconsistent in this regard [8, 15–19]. The European Society of Cardiology (ESC) recommends UFH as the first line prophylaxis early after SVR, while subcutaneous low molecular weight heparin (LMWH) is considered as off-label [16]. There is a growing body of evidence from observational studies that suggests that prophylaxis with LMWH after SVR is as safe and as effective as UFH while also having an advantage of easier administration [1, 9–11]. The optimal dosage and timing of LMWH initiation after SVR remains unknown. There are scant evidence-based recommendations available for periprocedural antithrombotic prophylaxis in surgical valvuloplasty [16]. Adequate periprocedural antithrombotic prophylaxis in patients undergoing SVR is an unmet clinical need that requires further investigation.

Therefore, this study aims to evaluate the safety and efficacy of periprocedural LMWH and to determine optimal dosage and timing of LMWH cessation before and initiation after surgical valve procedures (SVP).

Methods

This was a single-center, retrospective observational analysis. All consecutive patients who underwent elective SVP including SVR, valvuloplasty, combined valve procedure with coronary artery bypass grafting (SVP+CABG), or with concomitant ascending aorta replacement between January 2015 and January 2016 were included. Patients who required aortic valve replacement due to aortic dissection, periprocedural intra-aortic balloon counter pulsation or hemodialysis due to severe perioperative renal insufficiency were excluded. Prosthesis selection (biological vs. mechanical) was based on currently recommended consensus guidelines, including previous indications for chronic anticoagulation [16]. Surgical procedures were performed with UFH to maintain an activated clotting time (ACT) above 400 s during CPB. After the procedure, protamine sulfate was given for reversal of UFH in a 0.8–1:1 ratio. In the event of an ACT > 130 s during postoperative recovery, additional doses of protamine or tranexamic acid were administered at the surgeon's discretion. Two or three surgical drains (36 French) were placed around the heart and in the pleural cavities. Unless the drainage was not increased, drains were removed 1 day after SVP. Patients stayed in the intensive care unit or step-down unit until the second postoperative day. The two epicardial electrodes placed during SVR were removed on the third postoperative day.

The present institutional protocol herein, for periprocedural antithrombotic prophylaxis, consisting of LMWH therapy without anti-Xa factor monitoring, was utilized for all patients included in the present analysis. The timing of cessation, timing of initiation, and dosage of LMWH before and after SVP were based on current guidelines and individualized based on the surgeon's discretion, type of procedure, degree of achieved hemostasis, patient clinical condition, thromboembolic risk, body weight, and renal function [8, 15–19]. In the current protocol, LMWH was started 8–12 h after SVP with prophylactic dosages of 40–60 mg on the day of SVP and 40–80 mg on the first postoperative day, and then therapeutic dosages at 12-h intervals from the second postoperative day onwards. Oral anticoagulation (OAC) prophylaxis was started between the second and third postoperative days, after drains were removed as per patient clinical condition. LMWH was administered until the patient's international normalized ratio (INR) was within a therapeutic range (2–3 after aortic valve replacement, 2.5–3.5 after mitral or tricuspid valve replacement).

Early antiplatelet prophylaxis with acetylsalicylic acid (ASA; 150 mg/day) was prescribed in cases of aortic bioprosthesis implantation, starting on SVP day, always in combination with LMWH

during the early post-procedural period. In cases of concomitant atrial fibrillation. LMWH/OAC monotherapy was recommended. Combined prophylaxis of LMWH/OAC with antiplatelet therapy (ASA/clopidogrel) was prescribed in cases of mechanical prosthesis implantation with CABG, recently performed percutaneous coronary intervention (PCI), or known peripheral arterial disease. In cases of bleeding early after SVP, antithrombotic prophylaxis with LMWH or antiplatelet agents was started after the achievement of proper hemostasis, in accordance with the aforementioned standardized criteria.

The outcomes evaluated in this investigation were in-hospital bleeding, transfusions (packed red blood cells, platelet concentrate, or fresh frozen plasma), reoperation due to bleeding, and thromboembolic events. The risk factors evaluated in this investigation were periprocedural prophylaxis with LMWH and OAC, differing dosage of LMWH (mg/day) used before and after SVP, and timing of LMWH/OAC cessation and initiation before and after SVP (day). Additionally, the impact of procedure related parameters were assessed, such as dosage of UFH (IU) administered during the procedure, dosage of protamine at the end of SVP (mg), two subsequent ACT measurements after UFH and protamine administration, time on CPB (min), aorta clamping time (min), and arterial blood gas analyses before and after CPB. Preoperative and postoperative data were collected from patient medical history. Detailed information regarding procedures were obtained from reviews of patient medical records.

All outcomes were assessed as in-hospital events and defined according to guidelines for reporting mortality and morbidity after cardiac valve intervention with the exception of bleeding [20]. Bleeding was defined according to the universal definition of perioperative bleeding in adult cardiac surgery, including moderate, severe and massive events (class 2–4) [21]. Although transfusion and reoperation due to bleeding are components of the bleeding definition, we also adopted these variables as separate endpoints. Thromboembolic events included prosthetic valve thrombosis, pulmonary embolism, peripheral thromboembolic events, stroke or transient ischemic attack.

Statistical analysis

Categorical data are presented as numbers and percentages. Continuous data are presented as mean ± standard deviation. Comparisons were made using the χ^2 or two-sided Fisher exact test for categorical variables. Continuous data were compared using the Student t-test and Wilcoxon test, depending on their distribution as assessed by the Shapiro-Wilk test. The association between risk factors and outcomes were performed using univariate and multivariable logistic regression analysis to estimate an odds ratio (OR) and its 95% confidence interval (CI). Additionally, the impact of LMWH and OAC dosage and timing of initiation and cessation on endpoints was assessed through a receiver operating characteristic (ROC) curve and by estimating its area under the curve (AUC) and 95% CI. The optimal values for LMWH and OAC cut-off were chosen by taking into account the greatest sum of sensitivity and specificity. The predictive values of dosage and timing of LMWH/OAC cessation and initiation were adjusted for potential confounding variables (**Suppl. Table 1**). Laboratory parameters were assessed on the day of SVP pre-procedure. A p-value < 0.05 was considered significant. All tests were performed using MEDcalc (Medcalc Software 2014). This study was approved by the Local Ethics Committee.

Results

This study included 388 consecutive SVP patients with a mean age of 63.6 ± 12.6 years. Among the 271 (69.84%) patients who underwent SVR, 161 (62.11%) patients received a mechanical prosthesis. Mechanical prostheses were implanted in mitral and aortic position in 42 (10.82%) and 119 (30.67%) patients, respectively. The baseline characteristics of the study population and type of procedures performed are presented in Table 1.

Early bleeding occurred in 153 (39.33%) patients, being severe and massive only in 37 (9.45%) and 14 (3.61%) cases, respectively. Reoperation due to bleeding was required in 25 (6.45%) patients and was 2.5 ± 5.03 days after SVP. Transfusions were required in 203 (52.32%) patients. The first transfusion event was mainly performed during or early after SVP (0.59 ± 0.97 days). Thromboembolic events were diagnosed in only 7 (1.8%) patients — all of them were early post-procedural strokes or transient ischemic attacks. Four (1.03%) deaths occurred during hospitalization. Two of the deceased had bleeding early after SVP, although bleeding was not the cause of death for any of them. Hospitalization time ranged between 4 and 30 days (mean 7.64 ± 2.92 days), and was significantly longer in those who bled (OR 1.19; 95% CI 1.09–1.29; p = 0.001). All procedural and in-hospital outcomes are presented in **Supplementary Table 1**. The

Table 1. Baseline clinical characteristics of study population (n = 388).

Age [year]	20–85 (63.6 ± 12.57)
≥ 65 years	224 (57.73%)
Female sex	160 (41.23%)
NYHA class:	
I	34 (8.76%)
II	113 (29.13%)
III	225 (57.99%)
IV	16 (4.12%)
Coronary artery disease*	177 (45.62%)
Previous MI	80 (20.62%)
Previous coronary intervention:	95 (24.48%)
PCI ≤ 6 months pre-TAVI	28 (7.22%)
CABG	9 (2.32%)
COPD	25 (6.44%)
Atrial fibrillation	110 (28.35%)
Diabetes mellitus	71 (18.30%)
Hypertension	293 (75.51%)
Renal failure**	27 (6.96%)
Liver failure	19 (4.90%)
History of bleeding	48 (12.37%)
Heart failure***	253 (65.21%)
Previous stroke/TIA	25 (6.44%)
Laboratory parameters before procedure:	
Hemoglobin [g/dL]	7.4–19 (13.78 ± 1.68)
Platelet count [/μL]	114–572 (206 ± 68)
INR	0.83–1.8 (1.03 ± 0.14)
APTT	20.8–77.7 (31.06 ± 6.16)
GFR [mL/min/1.73 m^2]	22.78–76.6 (49.54 ± 21.9)
Creatinine [mg/dL]	0.52–2.35 (1.15 ± 2.75)
Type of the procedure:	
Multi-SVP	62 (6.70%)
AVR	75 (19.32%)
SVR + ascending aorta replacement	26 (6.7%)
SVP + CABG	53 (13.65%)
MVpl	24 (6.18%)
MVR	55 (14.17%)
TVpl	2 (0.5%)
Mechanical prosthesis:	161 (62.11%)
Mitral/Aortic	42 (10.82%)/119 (30.67%)
Biological prosthesis:	110 (28.35%)
Mitral/Aortic	30 (7.73%)/80 (20.61%)

Data are shown as means ± standard deviation or number (percentage). *Stenosis > 50%, **GFR < 60 mL/min/1.73 m^2 or ≥ 200 mmol/L, detected in consecutive, in-hospital testing, prior to TAVI, or previously diagnosed and treated chronic renal failure; ***Left ventricular ejection fraction < 60%. APTT — activated partial thromboplastin time; AVR — aortic valve replacement; CABG — coronary artery bypass grafting; COPD — chronic obstructive pulmonary disease; GFR — glomerular filtration rate; INR — international normalized ratio; multi-SVP — multiple valve procedures; MI — myocardial infarction; MVpl — mitral valve annuloplasty; MVR — mitral valve replacement; NYHA — New York heart Association; PCI — percutaneous coronary intervention; SVR + CABG — valve procedures and coronary artery bypass graft combined procedure; TAVI — transcatheter aortic valve implantation; TIA — transient ischemic attack; TVpl — tricuspid valve annuloplasty

impact of patient characteristics, type of procedure, and basic laboratory parameters on endpoints are presented in **Supplementary Table 2**. Periprocedural antithrombotic prophylaxis in the study population and its impact on outcomes is presented in Figure 1.

Acetylsalicylic acid was the most commonly used antiplatelet agent pre-procedure (44.6% of patients), and after SVP (56.7% of patients). Clopidogrel premedication was used in 36 (9.3%) patients and significantly increased the risk of re-operation due to bleeding (p = 0.04). No significant association between LMWH and OAC before SVP was found with any endpoint. Similarly, early post-procedural LMWH prophylaxis had no impact on endpoints. Post-procedural OAC prophylaxis was significantly associated with reduced risk of bleeding (p = 0.002), transfusion (p = 0.004), and re-operation due to bleeding (p = 0.029), without affecting the risk of thromboembolic events (p = 0.20). Impact of dosage and timing of initiation and cessation of LMWH/OAC on endpoints are presented in Figures 2–5.

Higher dosage of LMWH before SVP was an independent risk factor for bleeding and transfusion, with > 60 mg/day as a predictor for these events (Figs. 2, 3).

Receiving the first dose of LMWH on the day of SVP was an independent predictor of bleeding, transfusion and reoperation due to bleeding with > 40 mg/day as a predictor for these events (Figs. 2, 4).

Administration of LMWH within 24 h before SVP increased the risk of transfusion. Similarly, cessation of OAC within fewer than 7 days before SVP, increased the risk of transfusion and reoperation (Fig. 5). In line with these results, higher INR before SVP increased the risk of bleeding and transfusion (**Suppl. Table 2**). Time of LMWH initiation after SVP was significantly associated with the risk of bleeding (OR 2.110; 95% CI 1.359–3.287; p = 0.001) and blood transfusion (OR 2.504; 95% CI 1.546–4.055; p < 0.001). Similarly, time of OAC initiation after SVP was associated with risk of blood transfusion (OR 1.805; 95% CI 1.298–2.510; p < 0.001).

Various procedural parameters were also found to be relevant study endpoints.

Each additional minute on CPB significantly increased the risk of bleeding (OR 1.017; 95% CI 1.003–1.032; p = 0.02) and transfusion (OR 1.021; 95% CI 1.004–1.038; p = 0.014). Furthermore, a correlation was found between higher dose of protamine at the end of SVP and blood transfusion early after surgery (OR 1.002; 95% CI 1.0–1.004;

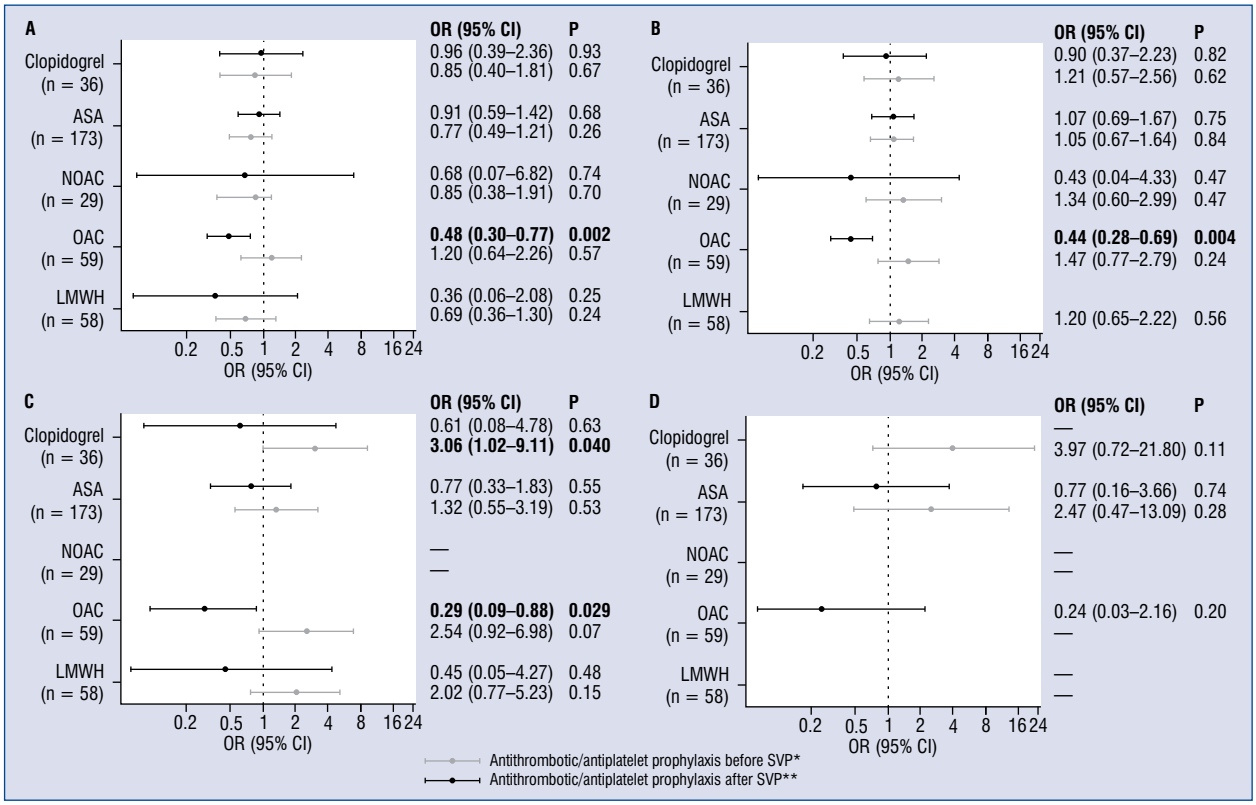

Figure 1. Impact of periprocedural antithrombotic/antiplatelet therapy on study endpoints in multivariate logistic regression analysis; **A.** Bleeding (n = 153); **B.** Transfusions (n = 203); **C.** Reoperation (n = 25); **D.** Thromboembolicevents (n = 7); *Combined therapy before SVP: dual antiplatelet therapy 15 (3.8%) patients, triple antithrombotic therapy 7 (1.8%) patients, LMWH/OAC/NOAC + ASA/clopidogrel 33 (8.5%) patients; **Combined therapy after SVP: dual antiplatelet therapy 14 (3.6%) patients, triple antithrombotic therapy 4 (1.0%) patients, LMWH/OAC/NOAC + ASA/clopidogrel 54 (13.9%) patients as only 7 thromboembotic events occur, we were able to produce only 4 OR in panel D; ASA — acetylsalicylic acid; CI — confidence interval; LMWH — low molecular weight heparin; NOAC — non-vitamin K antagonists oral anticoagulant; OAC — oral anticoagulation; OR — odds ratio; SVP — surgical valve procedures.

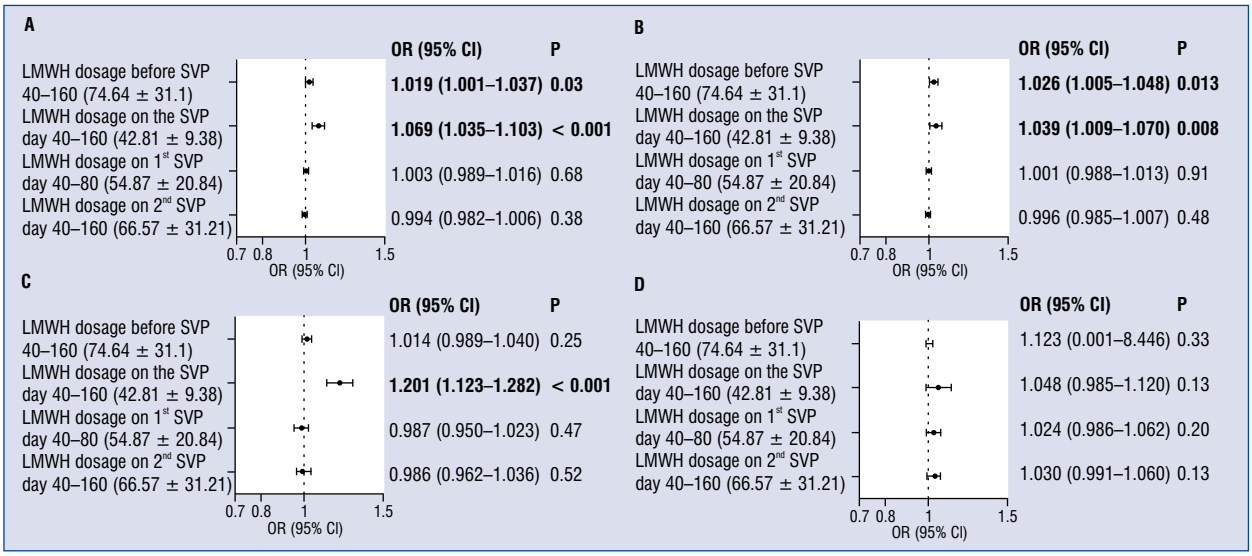

Figure 2. Impact of dosage of low molecular weight heparin (LMWH) and oral anticoagulation before and after surgical valve procedures on study endpoints in multivariate logistic regression analysis; **A.** Bleeding (n = 153); **B.** Transfusions (n = 203); **C.** Reoperation (n = 25); **D.** Thromboembolic events (n = 7). As only 7 thromboembolic events occured, the first OR in panel D for LMWH dosage before surgical valve procedures is only displayed in numbers to avoid modify the scale x axis; CI — confidence interval; OR — odds ratio.

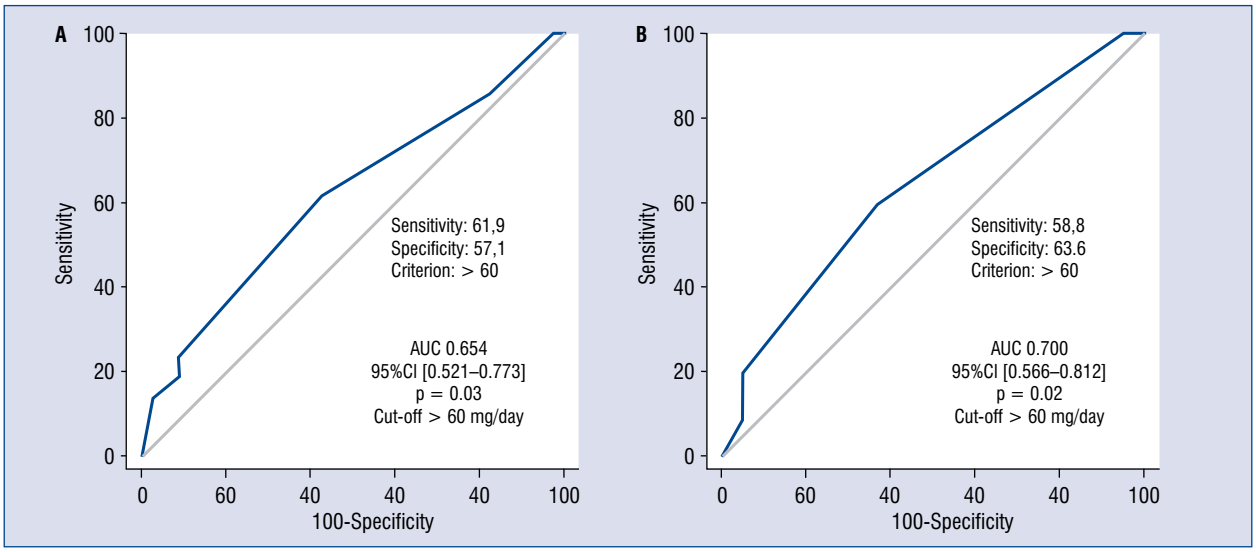

Figure 3. Impact of low molecular weight heparin (LMWH) dosage administered before surgical valve procedures on the study endpoints; **A.** Impact of LMWH dosage premedication on bleeding; **B.** Impact of LMWH dosage premedication on transfusion.

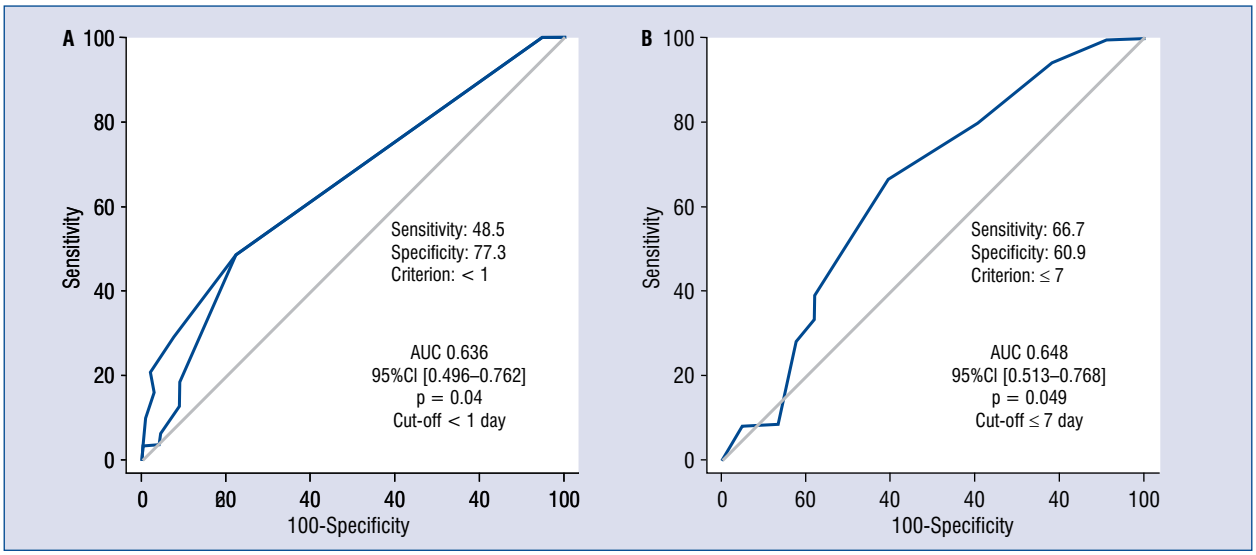

Figure 4. Impact of low molecular weight heparin (LMWH) and oral anticoagulation (OAC) time of cessation before surgical valve procedures on transfusion; **A.** Impact of LMWH cessation before SVP on transfusion; **B.** Impact the day of OAC cessation before SVP on transfusion

p = 0.04). Activated clotting time after UFH administration associated with bleeding (OR 0.997; 95% CI 0.995–0.999; p = 0.004) and thromboembolic events (OR 1.006; 95% CI 1.0–1.011; p = 0.048).

Discussion

The primary purpose of early prophylaxis after SVP is the prevention of valve thrombosis and thromboembolic events, which may be a result of temporal immobility of post-procedure patients [2, 8, 15–19]. Many experimental studies have suggested a postprocedural hypercoagulable state due to enhanced activation of plasma coagulation factors and platelets by surgically injured native heart tissue, turbulent flow across the prosthesis, and thrombogenicity of prosthesis artificial materials [1]. The necessity of chronic OAC prophylaxis

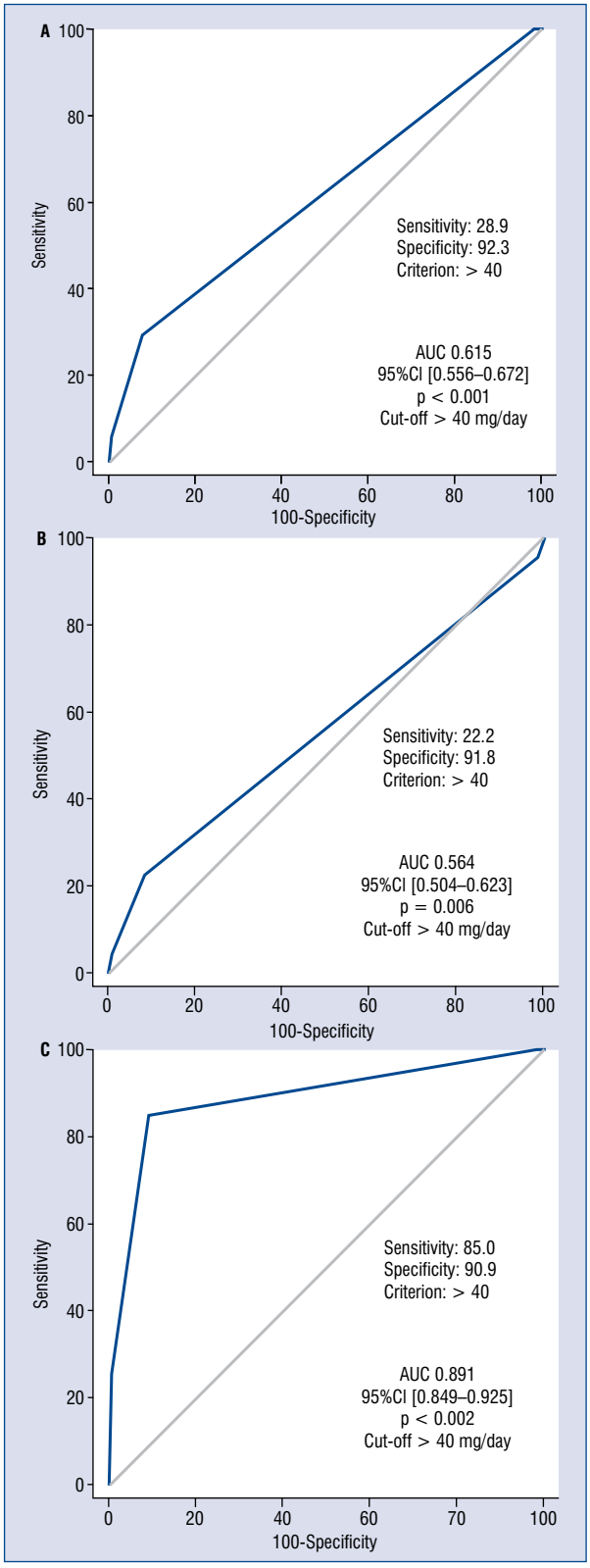

Figure 5. Impact of low molecular weight heparin (LMWH) dosage administered within 24 h after surgical valve procedures on the study endpoints; **A.** Impact of LMWH dosage on SVP day on bleeding; **B.** Impact of LMWH dosage on SVP on transfusion; **C.** Impact of LMWH dosage on SVP day on reoperation.

after SVP is well accepted. Chronic OAC provides a 75% reduction in the incidence of early thromboembolic events [1, 8, 15–19]. However, optimal prophylaxis directly after SVP remains unclear, especially when considering serious bleeding complications are among the most frequently noted in-hospital complications [1, 2, 9–12].

In this study, serious bleeding affected 13% of patients within 72 h after SVP, whereas early valve thrombosis was not observed. The only embolic events were strokes noted in fewer than 2% of subjects. These results are consistent with other studies that report bleeding occurs at least twice as often as the thromboembolic events in first 3 days after SVP, and bleeding is also the main reason for early reoperation [1, 2, 9–11, 22–24].

A variety of periprocedural antithrombic prophylaxis protocols have been proposed [1, 2, 8–11, 15–19]. Currently, the most common antithrombotic prophylaxis regimens are: early postoperative bridging with LMWH or UFH started on the day of SVP with OAC on the first postprocedural day or early OAC monotherapy with no bridging treatment [1, 2, 9, 25–29]. There is insufficient evidence to support the use of one of these strategies early after SVP [1, 2, 9–11]. Therefore, current recommendations regarding antithrombotic prophylaxis early after SVP are divergent, and a lack of consensus remains [8, 15–19].

Of note, SVP with CPB is responsible for significant consumption coagulopathy [1, 13]. Although these hemostasis disturbances are gradually restored within subsequent days, they translate into high risk of bleeding early after SVP. Considering the hemostatic disorders related to the procedure and disproportionate risk of bleeding compared to valve thrombosis, current prophylactic strategies with therapeutic doses of anticoagulants may be overly aggressive [1, 11].

Surprisingly, despite the absence of strong evidence, ESC guidelines recommend UFH bridging with early OAC implementation, and describe LMWH early after SVP as off-label prophylaxis [16]. Notably, this recommendation is based mainly on empiric, single center data [16, 29]. On the other hand, other guidelines and a substantial number of current reports suggest that LMWH after SVP is as effective as UFH and has a better safety profile than UFH, providing a rapidly achieved antithrombotic effect and predictable action without the necessity of routine laboratory monitoring [1, 9–11]. These advantages of LMWH translate into a shorter hospital stay and lower cost of hospitalization [1, 9–11].

The present study confirmed feasibility of LMWH early after SVP and described the most favorable dosage and timing of LMWH administration for optimal periprocedural prophylaxis. It was found that the most advantageous dosage of LMWH after SVP was 40–60 mg/day, which is equal to doses recommended for deep vein thrombosis prophylaxis after major surgery and for prolonged immobilization of high-risk patients [30]. Several other studies have also suggested the beneficial safety profile of prophylactic doses of heparins in comparison to therapeutic ones early after SVP, showing up to a fivefold reduction of major bleeding and a similar thromboembolic risk [1, 11].

Another insufficiently investigated concern is the safest time points for cessation and initiation of periprocedural antithrombotic prophylaxis with regard to SVP. The present results suggest that OAC should be stopped at least 6 days before SVP, while LMWH should be stopped 24 h preprocedure. These results are to some extent in agreement with guidelines that recommend stopping OAC 5 days before and LMWH between 12 and 24 h before major surgical procedures [8, 15–18].

Since this study found that dosage of LMWH on the day of SVP affected the safety outcomes, herein suggested, is the need for reassessment and special caution when considering LMWH initiation within the first 24 h of SVP. Furthermore, this especially deserves more attention given that consensus guidelines recommend considering longer delays in starting LMWH even up to 48–72 h after high bleeding risk procedures such as SVP [8, 15, 16, 18].

It is believed that the results of this study make several key contributions to the literature. Firstly, the present outcomes highlight the hemostatic profile of the SVP population in the first 72 h post-procedure, suggesting that in this period, hemostasis risk is tilted more toward bleeding than valve thrombosis. Secondly, in line with concern for increased bleeding risk, it is shown herein, that if a LMWH strategy is utilized, the most suitable approach is to use the reduced dose of LMWH as is recommended for prophylaxis of deep vein thrombosis equally before and after surgery. Similarly, as in previous studies, the present results highlight the presence of risk factors, which can modulate the safety and efficacy of antithrombotic prophylaxis. It is shown that a higher number of implanted prostheses; combined procedures, age, female sex, and New York Heart Association class of heart failure had meaningful impact on clinical endpoints. CPB time, higher value of ACT directly after UFH administration, and protamine dose with safety endpoints.

Limitations of the study

This study has several limitations. Firstly, the analysis may have limited power considering the small sample size; therefore, results should be interpreted cautiously. Secondly, the study population was heterogeneous, since it included mechanical and biological prosthesis implantation, valvuloplasty, as well as procedures combined with CABG. Additionally, the rate of bleeding was higher than expected. Although only 13% of incidents were life-threatening or severe, the rate of bleeding described in this study is substantially higher than has been previously reported [1, 2, 9–11]. This might be explained by the high surgical risk of the study population and high rate of complex procedures — 29.9% of multi-VP, 25.7% of VP+CABG, 6.7% of Bentall procedure or replacement of ascending aorta as part of a combined surgery. This might also be due to the lack of a unified definition for bleeding and thromboembolic events related to SVP. While guidelines for reporting complications during long-term follow-up after SVP exist [20], these recommendations do not address early complications during index hospitalization, such as early prosthesis thrombus, pericardial effusion, cardiac tamponade or excessive post-procedural drainage. Thus, it was elected to define early bleeding as per the most recent unified definition of perioperative bleeding from the International Initiative for Hemostasis Management in Cardiac Surgery [21]. Finally, there was an inability to thoroughly assess the impact of time of LMWH and OAC initiation after SVP. the present results are inconclusive in this regard, since time of LMWH/OAC initiation after SVP was biased by procedure related events. Although, according to the protocol, the first dose of LMWH was to be administered 8–12 h after SVP or after hemostasis achievement, no patient who experienced bleeding during SVP had LMWH started within 48 h. Since early post-procedural prophylaxis was withheld in cases of procedure related bleeding, it was difficult to determine optimal time for LMWH/OAC initiation after SVP from this data. Future studies should seek to address these limitations in a larger, carefully selected patient population.

Conclusions

Bleeding complications are the major early clinical adverse events after surgical valve pro-

cedures. Safety and efficacy of LMWH periprocedural prophylaxis depends on dosage and time of its administration. The most optimal strategy for periprocedural antithrombotic prophylaxis in the SVP population appears to be LMWH at a dosage of 40–60 mg/day, in line with what is recommended for deep vein thrombosis prophylaxis, stopped at least one day prior to the procedure.

Conflict of interest: None declared

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