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Usefulness of Baseline Activated Clotting Time–Guided Heparin Administration in Reducing Bleeding Events During Transfemoral Transcatheter Aortic Valve Implantation

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Objectives This study sought to evaluate the impact of baseline activated clotting time (ACT)–guided heparin administration on major bleeding after transfemoral transcatheter aortic valve implantation (TAVI).

Background Bleeding after TAVI is frequent and associated with unfavorable prognosis. Proper intraprocedural heparin dose administration may reduce the risk of potential overdosing in this frail study group.

Methods Of the patients who underwent transfemoral TAVI in our center from November 1, 2007 to June 31, 2012, 362 were retrospectively analyzed. Because abnormally high baseline ACT values were noted, heparin was administered at the operator's discretion, according to baseline ACT (ACT-guided, n = 174) or patient's body weight (non–ACT-guided, n = 188). The primary study objective was 30-day major bleeding as defined by the Valve Academic Research Consortium criteria. Secondary objectives were any life-threatening, and minor bleeding, and other Valve Academic Research Consortium outcomes at 30 days.

Results Bleeding occurred in 167 (46.1%) patients; of these, 76 (21.0%) had major bleeding. The ACT-guided group had a significantly lower occurrence of major (7.5% vs. 33.5%, $p < 0.001$), life-threatening (12.1% vs. 20.2%, $p = 0.04$), and any bleeding (25.9% vs. 64.9%, $p < 0.001$). Conversely, no differences were noted in the other study objectives. After adjustment for potential confounders, the protective odds ratio for ACT-guided therapy on major bleeding was 6.4 (95% confidence interval: 2.3 to 17.9; $p < 0.001$) at 30 days.

Conclusions In our experience, heparin administration according to baseline ACT was correlated with a significantly lower occurrence of major bleeding in transfemoral TAVI. This strategy might be a useful tool in reducing bleeding in this high-risk study group. (J Am Coll Cardiol Intv 2014;7:140–51) © 2014 by the American College of Cardiology Foundation

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Transcatheter aortic valve implantation (TAVI) has been demonstrated to be a valid therapeutic option for high-risk patients with symptomatic severe aortic stenosis (AS) (1,2). However, a wide range of potential complications might mitigate the beneficial effect of TAVI procedures. Particularly, TAVI-related bleeding still remains an important complication demanding careful consideration. Bleeding after TAVI is relatively frequent, ranging from 22.8% to 77.0%, and has been correlated with increased mortality (3–5). This is of particular concern in the TAVI study group mainly composed of elderly patients who are more prone to bleeding. Furthermore, patients with severe AS may have abnormalities in coagulation pathways as indicated by a higher incidence of spontaneous bleeding (6). The presence

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of severe comorbidities in this patient group, and the large sheath sizes required for arterial access are the main causes of bleeding complications after TAVI procedures. However, a common cause of bleeding in this study group might be represented by excessive intraprocedural anticoagulation therapy with heparin. According to the most recent expert consensus statement on TAVI, weight-based intravenous unfractionated heparin (UFH) is the recommended adjunctive intraprocedural antithrombotic therapy during TAVI with a suggested activated clotting time (ACT) >300 s throughout the procedure (7). On the other hand, an ACT target range of 250 to 300 s has been reported in the published data (8). Nevertheless, to the best of our knowledge, no study has specifically evaluated appropriate heparin dosing in this clinical setting. Because of the risk of potential overdosing with consequent hemorrhagic complications, strategies that provide a more accurate heparin dosing need to be investigated.

In our clinical practice, we systematically collected baseline ACT values during TAVI procedures, so we investigated a strategy where baseline ACT values were used for guiding subsequent heparin administration. Accordingly, the aim of the present study was to evaluate the impact of the baseline ACT-guided versus a non–ACT-based "weight-adjusted" heparin administration strategy on bleeding in transfemoral (TF) TAVI.

Methods

Study population. From November 2007 to June 2012, all consecutive patients with symptomatic severe AS treated with TF-TAVI in our center (San Raffaele Scientific Institute, Milan, Italy) were retrospectively analyzed. Patients were considered eligible for TAVI if they had a high or prohibitive risk for conventional surgery after being reviewed by a dedicated heart team, according to our current practice previously reported (9,10).

Procedures and devices. Depending on clinical conditions and evaluation of the patient by the cardiac anesthesiologist, the procedure was performed under either general or local anesthesia with conscious sedation. Both self-expanding and balloon-expandable prostheses were implanted. Initially, in November 2007, the Sapien THV (Edwards Lifesciences, Irvine, California) was used; the Medtronic CoreValve ReValving System (Medtronic, Minneapolis, Minnesota) valves became available in July 2008, and the Sapien XT replaced the Sapien THV in April 2010 (10). Details of the procedure were previously reported (9,10). In cases of full percutaneous TF approach, all therapeutic femoral access sites were closed with the Prostar (Abbott Vascular, Abbott Park, Illinois) pre-closure device. Moreover, the arterial access and closure of the access sites were performed with a "crossover technique" (11,12).

Heparin administration strategy: ACT versus non–ACT-guided group. As a standard practice used by our cardiac anesthetists, a baseline ACT measurement before administering heparin was performed in all patients undergoing TAVI procedures. ACT samples were drawn through the arterial sheath immediately after the insertion. To clear the sample from the flush solution contaminated by heparin, 10 ml of blood was withdrawn before taking the 4-ml ACT sample. ACT was measured using the Medtronic ACT Plus System.

Abbreviations and Acronyms

ACT = activated clotting time
AS = aortic stenosis
CI = confidence interval
IQR = interquartile range
IU = international units
OAT = oral anticoagulation therapy
OR = odds ratio
RBC = red blood cell
TAVI = transcatheter aortic valve implantation
TF = transfemoral
UFH = unfractionated heparin
VARC = Valve Academic Research Consortium

Interestingly, we noticed abnormally high values of baseline ACT in our study group. This observation raised the awareness of some operators who have started to administer the dosage of heparin on the basis of the baseline ACT values. Accordingly, on the basis of the operator's decision, in our series, 2 heparin administration strategies were performed: 1) an ACT-guided strategy in which heparin was adapted according to the baseline ACT; and 2) a non–ACT-guided strategy in which the heparin dosing was weight-adjusted. Details regarding the 2 heparin administration strategies are illustrated in Figure 1.

In both groups, the intraprocedural anticoagulant effect of the UFH was monitored and subsequently adjusted to maintain the ACT between 200 and 300 s. Heparin anticoagulation was reversed with protamine at neutralizing doses, if necessary, according to operator's preference.

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