Neutrophil to Lymphocyte Ratio and Risk of Atrial Fibrillation

We wish to commend the investigators of the article entitled "Relation of Neutrophil to Lymphocyte Ratio to Risk of Incident Atrial Fibrillation" by Berkovitch et al.[1] Neutrophils are known to play a role in the inflammatory response to injury[2] and the negative prognostic implications of elevated neutrophil values have been documented.[3] The ratio of neutrophils to lymphocytes however has been found to be a more sensitive predictor of outcomes in various clinical settings. The investigators examined the relation between neutrophil to lymphocyte ratio (NLR) and risk of atrial fibrillation (AF).

We have reported on the impact of elevated NLR on outcomes in 3,027 patients who underwent cardiac surgery.[4] Although AF was not one of our end points, we did find a higher incidence of AF at baseline (18% vs 12%, $p < 0.0001$) as well as a higher incidence of new AF after surgery (25% vs 21%, $p = 0.01$) in patients with elevated NLR. Elevated NLR was an independent predictor of adverse outcomes with over a twofold risk of operative mortality ($p < 0.001$). High NLR remained an independent predictor of reduced survival also in patients surviving surgery ($p = 0.0003$). We also examined the impact of elevated NLR in subgroups according to absolute neutrophil values: 81% were within normal range, 19% were above normal range. NLR was predictive of mortality in all these subgroups.

In this manuscript, patients with elevated NLR comprised 17% of the study population, not different from the incidence in our study. It is of interest in this present study, did the investigators analyze within the subgroups of neutrophils?

Despite rigorous preprocedural evaluation, we do not succeed in identifying all risk factors. NLR seems to unmask an increased risk of adverse outcomes, however, does not identify the underlying cause. Whether anti-inflammatory treatment will reduce risk is uncertain and remains a topic for further investigation.

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Outcomes and Resource Utilization for Nonelective Versus Elective Transcatheter Mitral Valve Repair

Transcatheter mitral valve repair (TMVr) has emerged as an effective treatment for severe mitral regurgitation (MR) in patients who are not suitable for surgical interventions.[1] Although the majority of patients undergo TMVr on an elective basis, many are referred for the procedure nonelectively due to decompensated heart failure. In the German TRAMI registry, 15% of patients underwent TMVr during nonelective hospitalizations.[2] Data from the early commercial experience with TMVr in the United States showed excellent short-term outcomes for patients who underwent TMVr overall, but did not assess the impact of presentation acuity on post-procedural outcomes.[1] We sought to investigate the incidence of nonelective TMVr and to compare in-hospital morbidity, mortality, resource utilization, and cost of elective versus nonelective TMVr using a nationally representative database.

Patients who underwent TMVr between January 1, 2011 and December 30, 2016 were identified in the National Inpatient Sample (NIS) using ICD-9-CM code (35.97) and ICD-10-CM code (02UG3JZ). The NIS is the largest public all-payer administrative database and contains information about discharges from 1,000 hospitals in 45 states representing 20% of all US hospitalizations. National estimates were calculated using the Agency for Healthcare Research and Quality weighting method, and those were used in all analyses. The procedure was classified as elective if the admission was assigned "elective" status in the NIS and TMVr occurred on day 0 or 1 of the admission. Patients with unknown procedure day or admission status were excluded. The primary outcome was in-hospital death. Secondary outcomes were postoperative complications, length of stay, rates of nonhome discharges, and cost. Outcomes were compared using chi-square test for categorical variables and independent samples t test for continuous variables. A type 1 error rate of <0.05 was considered statistically significant. Statistical analyses were performed using SPSS-version-24 (IBM corporation, Armonk, New York).

A total of 7,915 patients were included in the analysis of whom 6,329 (20%) were performed electively and 1,586 (20%) were performed during nonelective admissions. Patients who underwent nonelective TMVr were younger (72 ± 14 vs 77 ± 12 years), were less often of white race (72.1% vs 81.1%) and had higher prevalence of diabetes (30% vs 25%), chronic kidney disease (49.4% vs 25.9%), chronic lung disease (28.3% vs 23.5%), anemia (36.2% vs 22.8%), and atrial fibrillation (61% vs 56%), $p < 0.001$ for all. In-hospital mortality was higher in the nonelective group (6.9% vs 1.4%, $p < 0.001$). Rates of stroke, acute kidney injury, new dialysis, permanent pacemaker implantation, and blood transfusion were all significantly higher in the nonelective group which also experiences prolonged hospitalizations and a higher rate of nonhome discharge (Table 1). The mean cost of hospitalization in patients who underwent TMVr during nonelective admission was $\$77{,}861 \pm 69{,}118$, which was ~80% higher than the cost of hospitalization for elective TMVr.

The advent of TMVr has revolutionized the treatment of high-risk patients with severe MR. However, a significant percentage of those patients present acutely with decompensated heart failure.[1,2] Acute presentation has been

Table 1
In-hospital outcomes and resource utilization in patients who underwent elective versus nonelective transcatheter mitral valve repair

In-hospital outcome following TMVr	Elective (NE = 6,329)	Nonelective (NE = 1,586)	p Value
Death	1.4%	6.9%	<0.001
Stroke	0.8%	2.8%	<0.001
Pacemaker implantation	1.8%	7.9%	<0.001
Cardiac tamponade	0.5%	0.3%	0.4
New dialysis	0.7%	5.4%	<0.001
Acute kidney injury	9.0%	42.8%	<0.001
Blood transfusion	7.8%	19.0%	<0.001
Vascular complications	4.2%	7.3%	<0.001
Nonhome discharge	9.9%	33.1%	<0.001
Total LOS *Mean ± SD (Median/IQR)*	3.5 ± 4.1 (2,3)	15.8 ± 15.4 (12,10)	<0.001
Post-TMVr LOS *Mean ± SD (Median/IQR)*	3.2 ± 4.1 (2,3)	7.1 ± 7.2 (5,7)	<0.001
Cost *Mean ± SD*	43,219 ± 22,671	77,861 ± 69,118	<0.001

IQR = interquartile range; LOS = length of stay, SD = standard deviation; TMVr = transcatheter mitral valve repair.

shown to confer an excess operative risk in patients who underwent valvular heart surgery and transcatheter aortic valve replacement.[3–5] Data assessing the impact of incidence of acute presentation and its impact on the outcomes of TMVr are, however, limited. Our analysis documents that in early TMVr practice in the United States, a significant percentage (20%) of patients with severe MR undergo the procedure during an unplanned admission. Those patients have 4- to 5-fold higher in-hospital mortality, worse neurologic and renal outcomes, longer hospitalizations, and higher cost compared with patients who undergo TMVr electively. The excess cost accrued with nonelective TMVr has important financial implications, as current reimbursement for TMVr pose significant challenges to health care organizations attempting to deliver cost effective treatment even in elective cases. Further studies are needed to assess the role and cost effectiveness of TMVr in acutely decompensated patients.

Limitations

First, echocardiographic and procedural data are not available in the NIS and hence the success of TMVr in reducing MR could not be assessed in this study. Second, the NIS allows detailed assessment of hard clinical end points during the same hospitalization. However, outcomes beyond hospital discharge are not available. Third, the outcomes of acutely decompensated MR patients who did not undergo TMVr are not available. Hence, a comparative effectiveness analysis evaluating the impact of TMVr in these patients could not be performed.

Conclusions

One in 5 patients who underwent TMVr is referred for the procedure during a nonelective admission. Compared with elective TMVr, nonelective TMVr is associated with higher in-hospital morbidity, mortality, resource utilization, and cost. Further studies are needed to optimize the timing of TMVr and assess its role and cost effectiveness in acutely decompensated patients.

Disclosures

Dr. Alkhouli, Alqahtani, and Mathew have nothing to disclose. Dr. Bhatt discloses the following relations: Advisory Board: Cardax, Elsevier Practice Update Cardiology, Medscape Cardiology, Regado Biosciences; Board of Directors: Boston VA Research Institute, Society of Cardiovascular Patient Care, TobeSoft; Chair: American Heart Association Quality Oversight Committee; Data Monitoring Committees: Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute, for the PORTICO trial, funded by St. Jude Medical, now Abbott), Cleveland Clinic, Duke Clinical Research Institute, Mayo Clinic, Mount Sinai School of Medicine (for the ENVISAGE trial, funded by Daiichi Sankyo), Population Health Research Institute; Honoraria: American College of Cardiology (Senior Associate Editor, Clinical Trials and News, ACC.org; Vice-Chair, ACC Accreditation Committee), Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute; RE-DUAL PCI clinical trial steering committee funded by Boehringer Ingelheim), Belvoir Publications (Editor in Chief, Harvard Heart Letter), Duke Clinical Research Institute (clinical trial steering committees), HMP Global (Editor in Chief, Journal of Invasive Cardiology), Journal of the American College of Cardiology (Guest Editor; Associate Editor), Population Health Research Institute (for the COMPASS operations committee, publications committee, steering committee, and USA national co-leader, funded by Bayer), Slack Publications (Chief Medical Editor, Cardiology Today's Intervention), Society of Cardiovascular Patient Care (Secretary/Treasurer), WebMD (CME steering committees); Other: Clinical Cardiology (Deputy Editor), NCDR-ACTION Registry Steering Committee (Chair), VA CART Research and Publications Committee (Chair); Research Funding: Abbott, Amarin, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Chiesi, Eisai, Ethicon, Forest Laboratories, Idorsia, Ironwood, Ischemix, Lilly, Medtronic, PhaseBio, Pfizer, Regeneron, Roche, Sanofi Aventis, Synaptic, The Medicines Company; Royalties: Elsevier (Editor, Cardiovascular Intervention: A Companion to Braunwald's Heart Disease); Site Co-Investigator: Biotronik, Boston Scientific,

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