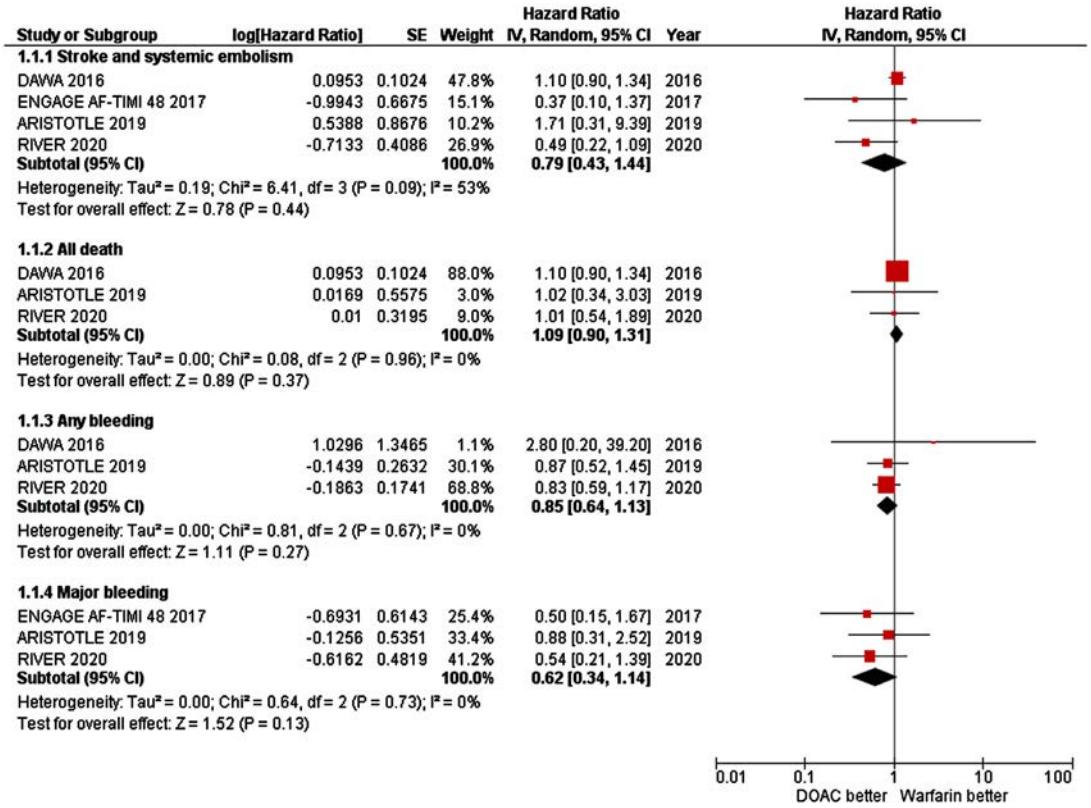

Figure 1. Forest plots of clinical outcomes. Abbreviations: ARISTOTLE: apixaban for reduction in stroke and other thromboembolic events in atrial fibrillations; DAWA: dabigatran versus warfarin after bioprosthesis valve replacement for the management of atrial fibrillation postoperatively; DOAC: direct oral anticoagulants; ENGAGE AF-TIMI 48: effective anticoagulation with factor Xa next generation in atrial fibrillationthrombolysis in myocardial infarction 48; RIVER: rivaroxaban for valvular heart disease and atrial fibrillations.

fibrillation postoperatively: DAWA pilot study. *Drugs R D* 2016;16:149−154.
5. Guimarães PO, Pokorney SD, Lopes RD, Wojdyla DM, Gersh BJ, Giczewska A, Carnicelli A, Lewis BS, Hanna M, Wallentin L, Vinereanu D, Alexander JH, Granger CB. Efficacy and safety of apixaban vs warfarin in patients with atrial fibrillation and prior bioprosthetic valve replacement or valve repair: insights from the ARISTOTLE trial. *Clin Cardiol* 2019;42:568−571.
6. Eikelboom JW, Connolly SJ, Brueckmann M, Granger CB, Kappetein AP, Mack MJ, Blatchford J, Devenny K, Friedman J, Guiver K, Harper R, Khder Y, Lobmeyer MT, Maas H, Voigt J-U, Simoons ML, Werf F Van de. Dabigatran versus warfarin in patients with mechanical heart valves. *N Engl J Med* 2013;369:1206−1214.

https://doi.org/10.1016/j.amjcard.2020.12.006

Change in Hospitalization Rates After Percutaneous Coronary Intervention for Chronic Total Occlusion (from a Nationwide Cohort Sample)

Successful percutaneous coronary intervention (PCI) for chronic total occlusion (CTO) has been associated with improvement of disabling anginal symptoms in patients with maximal medical therapy, improvement of left ventricular function, and reduces risk of ventricular arrhythmias.[1] Despite these benefits, patients continue to suffer from high hospitalization rates post-CTO PCI with chest pain being the most common cause.[2] In order to better understand the influence of CTO PCI on hospitalization rates, we aimed to explore the change in hospitalization rates pre- and post-CTO PCI by using the Nationwide Readmission Database (NRD).

NRD is a deidentified publicly available all-payers discharge database accounting for 58.2% of US hospitalizations.[3] By utilizing ICD-9/10 codes, we identified hospitalized patients with a diagnosis of CTO and underwent a single-vessel PCI during the same index admission from 2010 to 2017. We excluded patients with a diagnosis of acute coronary syndrome (ST-elevation or non-ST-elevation myocardial infraction (MI), and unstable angina). This approach was designed before to identify patients undergoing CTO PCI using administrative database.[4] We excluded patients who died during index admission and were admitted January-March or October-December in each year to capture 90-day follow-up before and after index admission since NRD data do not cross the calendar year.[5] The primary outcome was the change in 90-day all-cause hospitalization rate pre- and post-CTO PCI. The secondary outcomes included: (1) Change in 90-day hospitalization rates for heart failure, acute MI, chest pain without MI, and ventricular tachycardia-related hospitalizations; (2) a 30-day time frame analysis for the 90-day all-cause hospitalization rates pre- and post-CTO PCI; (3) change in all-cause 90-day hospitalization rates among key subgroups (Figure 1A). McNemar test was used to compare the hospitalization rates pre- and post-CTO PCI. A p value <0.05 was considered statistically significant. This study was exempted by the institutional review board due to the deidentified nature of the database.

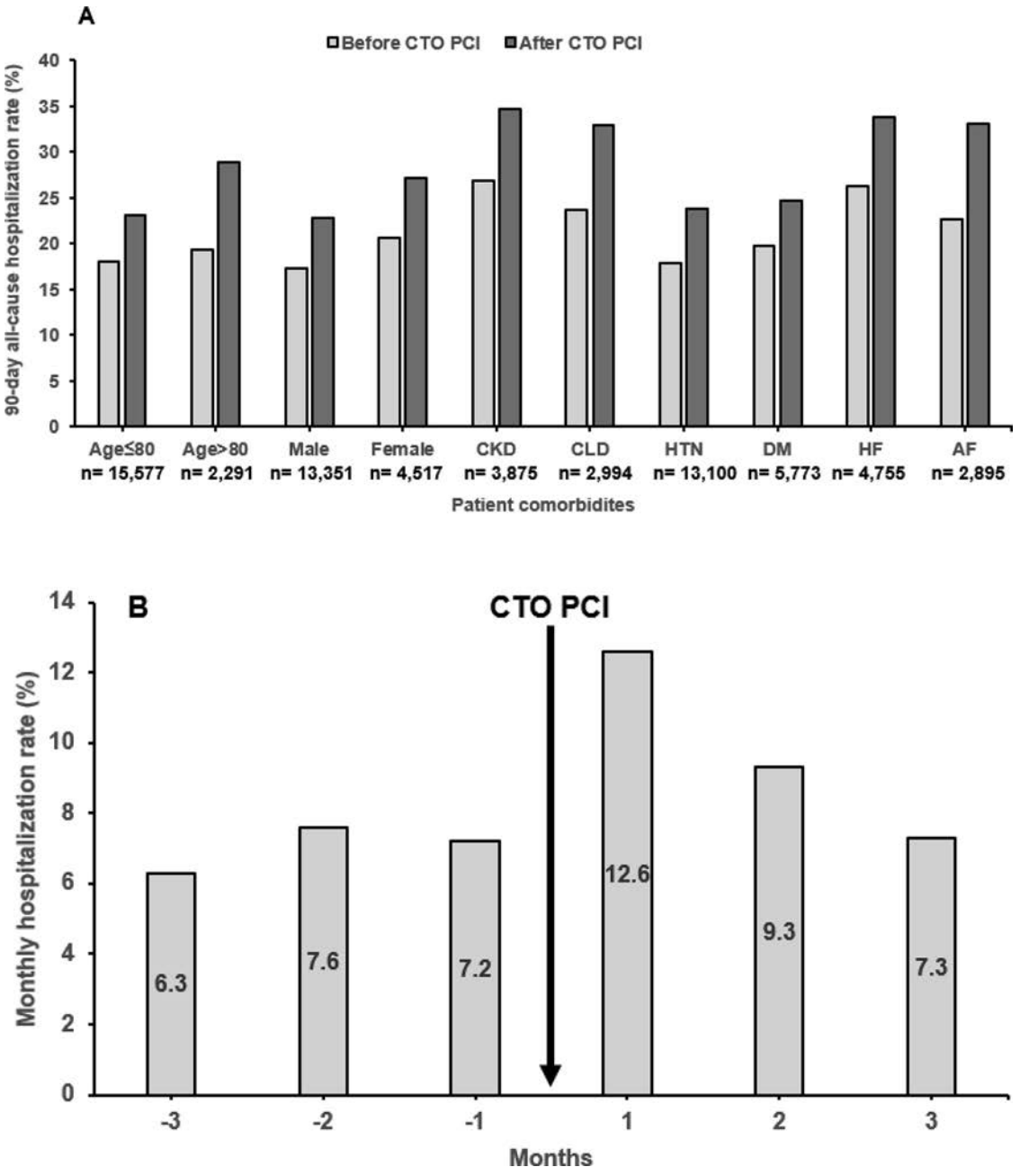

Figure 1. Hospitalization rates before and after percutaneous coronary intervention (PCI) for chronic total occlusion (CTO)
(A) A 90-day all-cause hospitalization rates pre- and post-CTO PCI among key subgroups. p value for all-comparison <0.001. AF = atrial fibrillation; CKD = chronic kidney disease; CLD = chronic lung disease; DM = diabetes mellitus; HF= heart failure; HTN = hypertension.
(B) Monthly all-cause hospitalization rate pre- and post-CTO PCI.

Analytic cohort of 17,868 patients met our inclusion criteria. The 90-day all-cause hospitalization rate pre- and post-CTO PCI increased from 18.1% to 23.8% (p <0.001). A similar pattern of change was observed across the examined subgroups (Figure 1A). The change in 90-day hospitalization rates pre- versus post-CTO PCI for: Heart failure 1.7% versus 1.8% (p = 0.635), acute MI 2.2% versus 1.3% (p <0.001), chest pain without MI 0.8% versus 1.0% (p = 0.011), and ventricular tachycardia-related hospitalization 0.2% versus 0.4% (p <0.001). The 30-day interval hospitalization rates over 90-day before and after the procedure showed a significant rise in the first 30-day post-CTO PCI (Figure 1B).

This nationwide observational analysis showed that CTO PCI was not followed by a reduction in 90-day all-cause, heart failure, chest pain without MI or ventricular tachycardia hospitalization rates, although a reduction in acute MI-related hospitalizations was noticed. The first 30-day post-CTO PCI was associated with the highest rate of hospitalization rate. Despite the known symptomatic improvement of the anginal symptoms and improvement of LV systolic function after CTO PCI, our study identified increased health care

utilization. Further studies are needed to investigate methods to reduce post-CTO PCI hospitalizations in order to maximize the benefits from the procedure.

These results should be cautiously interpreted in the context of limitations for using administrative database to identify CTO PCI. First, we cannot ensure the success of the procedure which may affect the postprocedure readmission rates however this is likely a small number, and that does not explain the increase in the hospitalization rates post-CTO PCI. Second, we may have captured non-CTO PCI patients; however it is less likely since we limited our cohort to a single-vessel PCI, excluded patients with ACS event, and the current practice paradigm favors coronary artery bypass graft for patient with multivessel coronary artery disease.[4] Finally, this analysis is restricted to inpatient procedures only, and does not capture outpatient CTO PCI, which is a big portion of this patient population with a possible different patient risk profile between both groups.

Funding

Self-funded.

Disclosure

The authors have nothing to disclose, and no relationship with industry.

Ahmed Elkaryoni, MD[a]
Islam Y. Elgendy, MD[b]
Ivo Genev, MD[c]
Mahmoud Khalil, MD, MSc[d]
Amir Darki, MD, MSc[ac*]

[a] Division of Cardiovascular Disease, Loyola University Medical Center, Loyola Stritch School of Medicine, Maywood, Illinois
[b] Division of Cardiovascular disease, Weill Cornell Medicine-Qatar, Doha, Qatar
[c] Department of Internal Medicine, Loyola University Medical Center, Loyola Stritch School of Medicine, Maywood, Illinois
[d] Lincoln Medical Center, New York

30 November 2020

1. Brilakis ES, Mashayekhi K, Tsuchikane E, Abi Rafeh N, Alaswad K, Araya M, Avran A, Azzalini L, Babunashvili AM, Bayani B, Bhindi R, Boudou N, Boukhris M, NŽ Božinović, Bryniarski L, Bufe A, Buller CE, Burke MN, Büttner HJ, Cardoso P, Carlino M, Christiansen EH, Colombo A, Croce K, Damas de Los Santos F, De Martini T, Dens J, Di Mario C, Dou K, Egred M, ElGuindy AM, Escaned J, Furkalo S, Gagnor A, Galassi AR, Garbo R, Ge J, Goel PK, Goktekin O, Grancini L, Grantham JA, Hanratty C, Harb S, Harding SA, Henriques JPS, Hill JM, Jaffer FA, Jang Y, Jussila R, Kalnins A, Kalyanasundaram A, Kandzari DE, Kao HL, Karmpaliotis D, Kassem HH, Knaapen P, Kornowski R, Krestyaninov O, Kumar AVG, Laanmets P, Lamelas P, Lee SW, Lefevre T, Li Y, Lim ST, Lo S, Lombardi W, McEntegart M, Munawar M, Navarro Lecaro JA, Ngo HM, Nicholson W, Olivecrona GK, Padilla L, Postu M, Quadros A, Quesada FH, Prakasa Rao VS, Reifart N, Saghatelyan M, Santiago R, Sianos G, Smith E, C Spratt J, Stone GW, Strange JW, Tammam K, Ungi I, Vo M, Vu VH, Walsh S, Werner GS, Wollmuth JR, Wu EB, Wyman RM, Xu B, Yamane M, Ybarra LF, Yeh RW, Zhang Q, Rinfret S. Guiding principles for chronic total occlusion percutaneous coronary intervention. *Circulation* 2019;140:420–433.
2. Sapontis J, Salisbury AC, Yeh RW, Cohen DJ, Hirai T, Lombardi W, McCabe JM, Karmpaliotis D, Moses J, Nicholson WJ, Pershad A, Wyman RM, Spaedy A, Cook S, Doshi P, Federici R, Thompson CR, Marso SP, Nugent K, Gosch K, Spertus JA, Grantham JA. Early procedural and health status outcomes after chronic total occlusion angioplasty: a report from the OPEN-CTO registry (outcomes, patient health status, and efficiency in chronic total occlusion hybrid procedures). *JACC Cardiovasc Interv* 2017;10:1523–1534.
3. Overview of the Nationwide Readmissions Database (NRD). Healthcare Cost and Utilization Project (HCUP). https://www.hcupus.ahrq.gov/nrdoverview.jsp.
4. Doshi R, Patel N, Kalra R, Arora H, Bajaj NS, Arora G, Arora P. Incidence and in-hospital outcomes of single-vessel coronary chronic total occlusion treated with percutaneous coronary intervention. *Int J Cardiol* 2018;269:61–66.
5. Elkaryoni A, Chhatriwalla AK, Kennedy KF, Saxon JT, Cohen DJ, Arnold SV. Change in hospitalization rates following transcatheter mitral valve repair: a nationwide cohort sample. *Circ Cardiovasc Interv* 2019;12:e008342.

https://doi.org/10.1016/j.amjcard.2020.12.011

The Chronic Kidney Disease Phenotype of HFpEF: Unique Cardiac Characteristics

Heart failure (HF) is highly prevalent in patients with chronic kidney disease (CKD), with HF with preserved ejection fraction (HFpEF) accounting for half of these cases.[1] CKD is independently associated with worse outcomes and higher mortality rates in patients with HFpEF.[2] With no proven therapies available to improve outcome in HFpEF patients, critical questions remain unsolved across the spectrum of HFpEF. One key question towards providing improved care for HFpEF is to discern whether subpopulations of HFpEF should be treated according to their pathophysiological phenotype. By assessing cardiac, exercise capacity, and body composition parameters and biomarkers, we aimed to characterize the phenotype of patients with HFpEF and CKD in order to identify pathophysiological mechanisms that are unique to this group.

Seventeen HFpEF patients with normal renal function (NRF) (Male/Female: 5/12; median [IQR] Age: 54 [50 to 60] years); N-terminal pro-brain natriuretic peptide (NTproBNP) 110 [48 to 255] pg/ml; estimated glomerular filtration rate (eGFR, by CKD EPI formula) 88 [75 to 96] ml/kg/1.73m^2) and 10 patients with HFpEF and CKD (Male/Female: 5/5; Age: 53 [47 to 67] years; NTProBNP 135.5 [33.0 to 333.3] pg/ml; eGFR 50 [42 to 57] ml/kg/1.73m^2) were studied. The investigation conformed with the principles outlined by the Declaration of Helsinki. Ethical approval was provided by the Virginia Commonwealth University Institutional Review Board and all participants provided written informed consent. A conservative ramping, maximal effort cardiopulmonary exercise test was performed on a treadmill as previously described.[3] Breath-by-breath gas analysis averaged over 10 seconds intervals was acquired with an automated gas analyzer to measure peak oxygen consumption (VO_{2peak}). Echocardiographic Doppler measures of systolic and diastolic function were performed at rest and at immediately postexercise. Measures included left ventricular ejection fraction, end-systolic volume index (LVESVI), end-diastolic volume index, mitral inflow velocities (E wave; A wave; E/A ratio; E wave deceleration time [DT]), early diastolic mitral annular velocity (e'), and e' indexed to DT (e'_{DT}). Diastolic function reserve index was calculated as $e'_{rest} \times \Delta e'_{exercise}$. Body composition was estimated by single-frequency bioelectrical impedance analysis. Self-reported functional status

This work was supported by National Institutes of Health [R34HL118348; UL1TR000058] and the American Heart Association [19CDA34740002 to DK; 19CDA34660318 to SC].