ISSN: 0975-3583,0976-2833 VOL16, ISSUE 1, 2025

PREDICTORS OF FAVOURABLE OUTCOME OF RADIAL ACCESS FOR PRIMARY ANGIOPLASTY IN A TERTIARY CARE CENTRE .

T Rajesh Sharma , Manoj Ravi , T.Govindan Unni , Prassannakumar C K, Bino Benjamin,

Resident, Department of Cardiology , JMMC&RC , Thrissur , Kerala
Consultant , Department of Cardiology , JMMC&RC , Thrissur , Kerala
Department of Cardiology , JMMC&RC , Thrissur , Kerala
Department of Cardiology , JMMC&RC , Thrissur , Kerala
Department of Cardiology , JMMC&RC , Thrissur , Kerala
Fax : +91 487 2421864
Corresponding Author :Dr Manoj Ravi
Mailing address – 2/875 Swathi , Nellikkunnu , East Fort PO , Thrissur . Pin – 680005
Phone – 9605005444, 9562275370
email –mrcardio@gmail.com ,nnped@yahoo.com
Fax - +91 487 2421864(office)

Abstract :

Primary percutaneous intervention is the preferred modality of treatment of patients with ST elevation myocardial infarction(STEMI). The complications with vascular access in radial route is less with experienced interventionist compared to the transfemoral route.The study aimed at assessing the procedure-related variables for a successful outcome of primary radial angioplasty and the outcome in the form of short term morbidity and mortality following procedure. While there were no complications in 80% cases ,local complications in 1.3% ,systemic complications contributed to short term morbidity . There were no mortality in the study population (n=315).The study emphasised the fact that primary angioplasty via radial route is safe in the hands of an experienced interventionist who has crossed the learning curve for the procedure.

Abbreviations – Primary percutaneous intervention PPCI ,Trans radial approach TRA , Trans femoral approach TFA ,ST elevation myocardial infarction STEMI

Keywords: Primary angioplasty , radial access , outcome , predictors

INTRODUCTION : PPCI is the preferred modality of treatment for patients with ST elevation myocardial infarction(STEMI). Advances in antiplatelet therapy and timely revascularisation has significantly reduced the mortality of STEMI. Post procedure bleeding has been linked to increased mortality in these patients and this include complications related to vascular access . Now , there are many studies advocating the lower risk associated with a trans radial access (TRA) for the procedure in terms of bleeding complications when compared to trans femoral approach(TFA) (3 ,2).Limitations of sample size and selection bias in those studies have led to two schools of thought regarding the route of choice for the procedure – transradial Vs transfemoral , since the first transradial successful procedure by Kiemeneij and Laarman in 1993 (3).

The aim of this study was to assess the procedure-related factors for a successful outcome in primary angioplasty following radial route.

ISSN: 0975-3583,0976-2833 VOL16, ISSUE 1, 2025

Aims of the study :

Primary Objective :

1.To evaluate the outcome of primary PCI through radial route in a tertiary care institution , in the form of complications in short term and all cause mortality following procedure.

For study purposes ,the primary outcome was defined as incidence of in-hospital (a) major and minor haemorrhages; (b) peri-procedural stroke; and (c) entry-site vascular complications. The secondary outcome was the incidence of in-hospital death and myocardial infarction/reinfarction taken together.

2.To identify the clinical and procedure-related variables associated with higher complication rates and a greater need for crossover rate.

Procedure related factors studied are : fluoroscopy time, contrast volume, and angioplasty success rate

Study design – Descriptive Observational study

Study Setting - Jubilee Mission Medical College & Research Institute,

Thrissur, Kerala, India

Study Duration: 16 months

Inclusion Criteria:

- All patients presenting with STEMI and being considered for primary PCI through radial access between January 2016 and January 2017.

Exclusion criteria:

- Patients with ACS other than STEMI
- All primary PCI in STEMI through femoral access.
- All radial elective PCI.

Sample size : Fixed at 400, only 315 subjects could be included during the study period , as per operator's comfort level in performing the procedure by trans radial route after assessing the risk status.

Materials & Methods

This was an observational study in patients with acute STEMI. Patients were enrolled in the study after obtaining informed written consent from the patient or relatives. The baseline demographic characteristics of above mentioned were recorded using a proforma. The study is conducted among patients with acute STEMI, considered for primary PCI through radial artery access at operator discretion. Approval was taken from the Institutional ethics committee.

Data of all patients with acute STEMI with primary PCI through radial access was evaluated for baseline characteristics and procedural success and complications including crossover rate.

The parameters studied included complete medical history, cardiovascular risk factors assessment, clinical examination, anthropometry, characteristics of index event. The patients

ISSN: 0975-3583,0976-2833 VOL16, ISSUE 1, 2025

were classified as high risk group based on the presence of the following unfavourable criteria : elderly (>75 years) , cardiogenic shock , severe left ventricular systolic dysfunction ,high-degree AV block , low body surface area ,multivessel PCI , diabetes mellitus , low body mass index (BMI) .All patients without these unfavourable criteria was classified as non – high risk group . This is followed by 12 lead ECG evaluation and 2D echocardiogram to evaluate ejection fraction and regional wall motion abnormalities (RWMA). The findings of CAG and procedure done were also studied. Patients in the prospective study were followed up till discharge and any in-hospital complication noted. All patients in the study are followed up as mentioned above.

Outcome

1.The patients who underwent the primary angioplasty through radial route were assessed for morbidity in the short term in the form of various complications.

2.The complications which lead to the unfavourable outcome , death were also sought for analysis.

The success of the procedure was defined as placement of stent in the target lesion successfully with residual diameter stenosis of < 10% and TIMI 3 flow without any major procedural complication or immediate post procedure adverse event like MI , acute stent thrombosis , need for emergency revascularisation or cardiac death.

Procedure was done through right radial artery in most of the cases, Radial artery was punctured after administration of local anaesthesia and 6Fr sheath inserted. 100 IU/kg body weight of heparin was administered during the procedure .Tiger catheter (Terumo) was the commonest diagnostic catheter used. EBU Launcher (Medtronic) was the commonest guiding catheter used for left sided intervention and JR Launcher (Medtronic) for the right coronary artery canulation. Pressure bandages were applied for hemostasis after sheath removal.

Results :

Table 1 Demographic characteristics

Variables		High Risk Group % (N=112)	Non-High risk Group % (N=203)	Total	
				N= 315	Percentage
Gender	Male	26.3	55.9	259	82.2

ISSN: 0975-3583,0976-2833 VOL16, ISSUE 1, 2025

	Female	9.2	8.6	56	17.8
Age	≤40	2.2	3.2	86	27.3
	41 -50	6.1	15.9		
	51 - 60	9.8	24.8	208	66
	61 - 70	7.6	17.5		
	71-75	3.2	3.2		
	>75	6.7	0		6.7
BMI	Underweight (BMI < 19)	5.1	7.9	41	13
	Normal (BMI 19 - 25)	22.9	40.9	201	63.8
	Overweight (BMI > 25)	7.6	15.6	73	23.2

Baseline characteristics

Average systolic BP was 140.8 ± 31.6 mmHg and diastolic BP was 83.4 ± 16.1 mmHg at presentation. Regarding area of infarction AWMI were present in 48.9% (q RBBB pattern in 4.5%) and IWMI spectrum in 51.1% (with 4.4% with RVMI). Echo showed normal LV function (LVEF >50%) in 22.9 %, mild LV systolic dysfunction (LVEF 40-50%) in 39.4%, moderate LV systolic dysfunction (LVEF 30-40%) in 18.7 and severe LV systolic dysfunction (LVEF< 30 %) in 19 %.

Table 2 : Morbidity profile of study

Risk Factors	**High Risk Group (N = 112)**	**Non High Risk Group (N = 203)**	**Total (N = 315)**
DM	13.9	28.5	42.5 (134)
HTN	13.3	26.1	39.4 (124)
DLP	3.8	7.3	11.1 (35)
H/O Vascular disease	3.2	3.5	6.7 (21)
Family history of premature CAD	2.5	4.2	6.7 (21)
Smoking	9.5	19.4	28.9 (91)

Table 3 : Comparison of Procedural parameters after randomization in both groups

TIMI Flow

ISSN: 0975-3583,0976-2833 VOL16, ISSUE 1, 2025

Parameters		High Risk Group (N=112)	Non-High Risk Group (N=203)	Total (N=315)	P value
TIMI flow	Grade 1	3	1	4 (1.27 %)	0.120
	Grade 2	17	23	40 (12.7 %)	
	Grade 3	92	179	271 (86.03 %)	

Fluroscopy time

Parameters		High Risk Group (N=112)	Non-High Risk Group (N=203)	Total (N=315)	P value
Fluroscopy time	**< 10**	**96**	**180**	**276 (87.6 %)**	**0.477**
	≥10	**16**	**23**	**39 (12.4 %)**	
T test (Comparison of means of fluoroscopy time among risk groups)					
Mean ± SD		6.44±4.18	6.34±3.55		**0.817**

Contrast volume

		High Risk Group (N=112)	Non-High Risk Group (N=203)	Total (N=315)	P value
Contrast Volume	**≤100**	**97**	**167**	**264 (83.5%)**	**0.465**
	100 – 150	**7**	**21**	**28 (9.2%)**	
	>150	**8 (34.8 %)**	**15 (65.2 %)**	**23 (7.3%)**	
T test (Comparison of means of contrast volume among risk groups)					
Mean ± SD		110.27±27.78	112.32±29.37	0.547	

Chi-square and T test showed no significant differences in procedural parameters among risk groups.

Procedural characteristics

Table 4 **Complications**

Complications	No high risk group	High risk group N=112	Total N=315	%

ISSN: 0975-3583,0976-2833 VOL16, ISSUE 1, 2025

	N=203			
None	171	81	252	80
With local complications	3	1	4	1.3
With systemic complications	29	30	59	18.7

Table 5 **Systemic complications**

	No high risk group N=203	**High risk group N=112**	**Total N=315**	**%**
Stroke /TIA	1	3	4	6.8
Pulmonary edema	0	3	3	5.1
Acute kidney injury (AKI)	16	11	27	62.7
AKI with arrhythmia	0	1	1	
Acute on CKD	5	3	8	
AKI with cardiac tamponade	1	0	1	
Resuscitated cardiac arrest	0	4	4	6.8
Arrythmias	0	2	2	3.4
Acute stent thrombosis (< 24hrs)	3	2	5	8.5
Primary VT, Temporary pacemaker insertion	2	1	3	5
GI bleed from haemorrhoids	1	0	1	1.7

Complications

Patients were followed up for any in-hospital complications (if any) till discharge. Complications were present in 20 % of patients. 18.7% patients had systemic complications and 4 patients had local complications. Acute kidney injury(AKI) was the most common systemic complication (62.7%). All the AKI patients completely recovered from AKI, except 2 patients with CKD requiring dialysis. Four (1.3%) patients had acute stroke and 1 patient

ISSN: 0975-3583,0976-2833 VOL16, ISSUE 1, 2025

had transient ishaemic attack(TIA). Four patients had cardiac arrest with primary VT/VF resuscitated during in hospital stay. Out of this 3 patients had acute pulmonary oedema.

Subgroup Analysis

112 patients were in high risk group and 203 patients in the non high risk group. There was no statistically significant differences between the high risk group and non high risk groups in terms of procedural variables and complications (p value >0.05)(Table4,Table 5) .

Statistical analysis

Data were expressed as the mean, standard deviation (SD) or percentage (%). High risk and non high risk groups were compared for different variables. A probability value of less than 0.05 was considered statistically significant.

Discussion :

Primary PCI through radial route was assessed for procedure related variables and predictive factors of favourable outcome in the present study . Majority of the subjects were males (82.2) and rest were females (17.2).The age group undergoing the procedure was >50 years in 66% . Most were having a normal BMI. Elizabeth Curtis etal reported a higher representation of males in their descriptive study population (59.8%). The procedure was described as a safe one with relatively lesser complications from beginning itself. The difficulty described by Kiemeneij F was access failure when they first reported the case done through radial route. Chugh SK has pointed out regarding the " learning curve" for radial angioplasty procedure describing it as requiring atleast a decade of practice to be an expert with the technique . While Elizabeth Curtis etal described that females with anxiety had more radial artery spasm , the analysis concluded that young age was a statistically important predictor of radial artery spasm . Proper premedication , more use of 5 Fr catheters with less manipulation by experienced interventionist might have been the reasons why this complication was not seen in this study.

81.3 % patients underwent the primary radial angioplasty without systemic complications in the present study .One of the earliest publication in 1997 by Kiemeneij etal itself had shown a success rate of 91.7% in the radial access group , higher than femoral or brachial route access for angioplasty.

This study provides valuable insights into the predictors of favorable outcomes with radial access for primary percutaneous coronary intervention (PCI) in patients with acute myocardial infarction. The key findings are as follows:

Morbidity profile: The study identified several important risk factors, including diabetes mellitus (42.5%), hypertension (39.4%), dyslipidemia (11.1%), and smoking (28.9%), that were prevalent in the study population. These findings are consistent with the known risk factors for coronary artery disease and the development of acute myocardial infarction(6,7).

Complications: Transfemoral approach is preferred in chronic total occlusion cases as access and procedural success was more when using large bore (>7Fr) catheters . Sheath – to – artery mismatch was more in smaller radial artery route procedures leading to bleeding and vascular complications . The availability of modern slender technology as thin-walled radial introducer sheath has brought down this risk considerably in trans radial procedures(8).This study reported a low overall rate of complications, with 80% of patients experiencing no complications, 1.3% with local complications. The most common systemic complications were acute kidney injury (62.7%), stroke/TIA (6.8%), and resuscitated cardiac arrest (6.8%). These findings highlight the importance of careful patient selection and meticulous

ISSN: 0975-3583,0976-2833 VOL16, ISSUE 1, 2025

procedural technique when performing radial access PCI, especially in high-risk patients(6,7,9,10).

The results of this study are consistent with the growing body of evidence supporting the use of radial access for primary PCI in patients with acute myocardial infarction. Several large-scale randomized trials and meta-analyses have demonstrated the benefits of radial access, including reduced bleeding complications, shorter hospital stay, and improved patient satisfaction, without compromising procedural success or clinical outcomes (6,7,9,10).

All the patients in the present study including those with systemic complications were discharged latest by 14th day post admission. Having no mortality in the sample achieved in the study period, we could infer that there is no increased all cause mortality when compared with the femoral procedure done by the interventionist in the same centre. This finding is proven in the MATRIX trial as well as in the SAFARI- STEMI randomised controlled trial by May ML et al. (6,10).The RIVAL trial and the –STEACS trial have concluded that STEMI patients have lesser mortality when undergoing the procedure via trans radial route (11).

Crossover to femoral approach in the study population was zero. Meijers TA et al had got a cross over rate of around 3.6% in a multicentric randomised trial of 388 patients. The difference could be in the fact that the procedure was performed in a larger sample by different interventionists(8)

The present study adds to this literature by providing a detailed analysis of the predictors of favorable outcomes with radial access in a real-world setting. The findings suggest that experienced operators can achieve similar procedural success and clinical outcomes with radial access, even in high-risk patients, by carefully selecting appropriate candidates and employing meticulous technique.

The success of procedure was defined by TIMI 3 flow and a reduction in the percentage diameter stenosis of < 10 % (14). The analysis of procedural parameters showed that TIMI 3 flow was achieved in 86.03% , TIMI 2 in 12.7% ,TIMI 1 in 1.27%.The procedure success rate is comparable to other randomised controlled trials comparing radial and femoral routes in different settings (8)

Procedural parameters: The study found no significant differences in procedural parameters such as TIMI flow, fluoroscopy time, and contrast volume between the high-risk and non-high-risk groups. This suggests that experienced operators can achieve similar procedural success rates with radial access, regardless of patient risk profile(8,9).

The randomised comparison by Michael T et al in 2013 had assigned more procedure time in trans radial procedures (15).But later in 2018 ,the meta analysis of 12 randomised controlled trials by Mohandes M et al found no increase in procedure time taken in trans radial procedures . This result might either be due to the crossing of learning curve for the procedures by interventionists over the years or due to the lack of common definition of operational time between various studies (16,17). In this study, majority of patients had fluoroscopy time < 10 minutes (87.6%) for the procedure.

The contrast volume used during the procedure was ≤ 100ml in 83.5%, 100-150 ml in 9.2% and more than 150 ml in the rest of the patients. Ahsan MJ et al has recently inferred that there is no significant difference in contrast volume used in transradial procedures when compared to transfemoral procedures(18).

In conclusion, this study highlights the feasibility and safety of radial access for primary PCI in patients with acute myocardial infarction, even in high-risk subgroups. The low rate of complications and the lack of significant differences in procedural parameters

ISSN: 0975-3583,0976-2833 VOL16, ISSUE 1, 2025

between risk groups underscore the importance of operator experience and patient selection in achieving favorable outcomes with this approach.

Limitations of the study was mainly the inability to achieve the sample size during the study period . The findings are not generalizable unless verified by a randomized controlled trial to assess the various factors studied in both trans femoral and transradial routes in the same study setting . The majority of study population were males(82.2%). Thus , the results may not be generalised for females .Another would be the bias in selection of patients as transradial route was chosen as per operator discretion. Here ,the risk-treatment paradox might have intervened and highest risk patients might have been excluded in the study with trans radial procedures and might have underwent procedure through transfemoral route.The operator's comfort level in performing the procedure might have excluded several of such high risk cases in the study period . Over the years , the acknowledgement that transfemoral route procedures carry higher bleeding and vascular complications risk has occurred . The same study would have probably included more patients of higher risk levels if done in recent times in the same institution . Amin AP et al had demonstrated that a risk treatment paradox exists for transradial procedures with not only bleeding risk , but also that of risk for AKI and mortality risks(19) . But the analysis of their study leads to the recommendation that trans radial route should be the choice even for higher risk cases to reduce adverse outcomes . Our data also shows that while some of the systemic complications were more in high risk group (18.7%), 80% of sample didn't have any complications at all. Thus , transradial route would be preferable in our population irrespective of risk levels as well.

References :

1. Généreux et al., "Radial Access in Patients with ST-Segment Elevation Myocardial Infarction Undergoing Primary Angioplasty in Acute Myocardial Infarction."
2. Pristipino et al., "Major Improvement of Percutaneous Cardiovascular Procedure Outcomes with Radial Artery Catheterisation."
3. Kiemeneij F, Laarman GJ, Odekerken D, Slagboom T, van der Wieken R. A randomized comparison of percutaneous transluminal coronary angioplasty by the radial, brachial and femoral approaches: the access study. J Am Coll Cardiol. 1997 May;29(6):1269-75. doi: 10.1016/s0735-1097(97)00064-8. PMID: 9137223. With experience, procedural and clinical outcomes of PTCA were similar for the three subgroups, but access failure is more common during transradial PTCA. Major access site complications were more frequently encountered after transbrachial and transfemoral PTCA.

4. Chugh SK. Trans-radial interventions - From 'Bandwagon' to 'Movement': Where we were; where we are and where do we go from here…. Indian Heart J. 2015 Nov-Dec;67(6):627-8. doi: 10.1016/j.ihj.2015.07.055. Epub 2015 Oct 26. PMID: 26702711; PMCID: PMC4699952. Radial is now a movement in the country. It will take a decade for anyone starting now to become an expert and take on angioplasty in acute coronary syndromes, where most of the benefit is and which is most of our work in India!

5. Goel PK, Jatain S, Khanna R, Pandey CM. Left main PCI: An observational analysis from large single-centre experience. Indian Heart J. 2016 Jan-Feb;68(1):36-42. doi: 10.1016/j.ihj.2015.07.010. Epub 2015 Aug 29. PMID: 26896264; PMCID: PMC4759493.

ISSN: 0975-3583,0976-2833 VOL16, ISSUE 1, 2025

6. Valgimigli, M., Gagnor, A., Calabró, P., Frigoli, E., Leonardi, S., Zaro, T., … & MATRIX Investigators. (2015). Radial versus femoral access in patients with acute coronary syndromes undergoing invasive management: a randomised multicentre trial. The Lancet, 385(9986), 2465-2476.

7. Romagnoli, E., Biondi-Zoccai, G., Sciahbasi, A., Politi, L., Rigattieri, S., Pendenza, G., … & Sangiorgi, G. M. (2012). Radial versus femoral randomized investigation in ST-segment elevation acute coronary syndrome: the RIFLE-STEACS (Radial Versus Femoral Randomized Investigation in ST-Elevation Acute Coronary Syndrome) study. Journal of the American College of Cardiology, 60(24), 2481-2489.

8. Meijers, T, Aminian, A, van Wely, M. et al. Randomized Comparison Between Radial and Femoral Large-Bore Access for Complex Percutaneous Coronary Intervention. *J Am Coll Cardiol Intv.* 2021 Jun, 14 (12) 1293–1303.

9. Jolly, S. S., Yusuf, S., Cairns, J., Niemelä, K., Xavier, D., Widimsky, P., … & RIVAL trial group. (2011). Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicentre trial. The Lancet, 377(9775), 1409-1420.

10. Le May, M. R., Wells, G. A., So, D. Y., Glover, C. A., Froeschl, M. P., Marquis, J. F., … & SAFARI-STEMI Investigators. (2020). Safety and efficacy of femoral access vs radial access in ST-segment elevation myocardial infarction: the SAFARI-STEMI randomized clinical trial. JAMA cardiology, 5(2), 126-134.

11. Le May M, Wells G, So D, et al. Safety and Efficacy of Femoral Access vs Radial Access in ST-Segment Elevation Myocardial Infarction: The SAFARI-STEMI Randomized Clinical Trial. *JAMA Cardiol.* 2020;5(2):126–134. doi:10.1001/jamacardio.2019.4852

12. Jolly SS, Yusuf S, Cairns J, et al; RIVAL Trial Group. Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicentre trial. *Lancet*. 2011;377(9775):1409-1420. doi:10.1016/S0140-6736(11)60404-2

13. Romagnoli E, Biondi-Zoccai G, Sciahbasi A, et al. Radial versus femoral randomized investigation in ST-segment elevation acute coronary syndrome: the RIFLE-STEACS (Radial Versus Femoral Randomized Investigation in ST-Elevation Acute Coronary Syndrome) study. J Am Coll Cardiol. 2012;60(24):2481-2489. doi:10.1016/j.jacc.2012.06.017

14. Brasselet C, Tassan S, Nazeyrollas P, Hamon M, Metz D. Randomised comparison of femoral versus radial approach for percutaneous coronary intervention using abciximab in acute myocardial infarction: results of the FARMI trial. Heart. 2007 Dec;93(12):1556-61.

15. Michael, T, Alomar, M, Papayannis, A. et al. A Randomized Comparison of the Transradial and Transfemoral Approaches for Coronary Artery Bypass Graft Angiography and Intervention: The RADIAL-CABG Trial (RADIAL Versus Femoral Access for Coronary Artery Bypass Graft Angiography and Intervention). J Am Coll Cardiol Intv. 2013 Nov, 6 (11) 1138–1144.

ISSN: 0975-3583,0976-2833 VOL16, ISSUE 1, 2025

16. Louvard Y, Pezzano M, Scheers L, Koukoui F, Marien C, Benaim R, et al. Coronary angiography by a radial artery approach: Feasibility, learning curve. One operator's experience. Arch Mal Coeur Vaiss. 1998;91:209–15.
17. Mohandes M, Rojas S, Guarinos J, Fernández F, Moreno C, Torres M, Cediel G, De Castro R, Bardaji A. Procedure Time Comparison between Radial Versus Femoral Access in ST-Segment Elevation Acute Myocardial Infarction Patients Undergoing Emergent Percutaneous Coronary Intervention: A Meta-analysis of Controlled Randomized Trials. Heart Views. 2018 Jan-Mar;19(1):1-7.
18. Ahsan MJ, Ahmad S, Latif A, Lateef N, Ahsan MZ, Abusnina W, Nathan S, Altin SE, Kolte DS, Messenger JC, Tannenbaum M, Goldsweig AM. Transradial versus transfemoral approach for percutaneous coronary intervention in patients with ST-elevation myocardial infarction complicated by cardiogenic shock: a systematic review and meta-analysis. Eur Heart J Qual Care Clin Outcomes. 2022 Sep 5;8(6):640-650. doi: 10.1093/ehjqcco/qcac018. PMID: 35460230; PMCID: PMC9442849.
19. Amin AP, Rao SV, Seto AH, Thangam M, Bach RG, Pancholy S, Gilchrist IC, Kaul P, Shah B, Cohen MG, Gluckman TJ, Bortnick A, DeVries JT, Kulkarni H, Masoudi FA. Transradial Access for High-Risk Percutaneous Coronary Intervention: Implications of the Risk-Treatment Paradox. J Am Coll Cardiol. 2021 Jul 27;78(4):341-354. doi: 10.1016/j.jacc.2021.05.011. Epub 2021 Jun 2. PMID: 34253050; PMCID: PMC8292524.