Determinants of Drug-Coated Balloon Failure in Patients Undergoing Femoropopliteal Arterial Intervention

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Abstract

Background: Drug-coated balloons (DCB) are frequently used to treat femoropopliteal artery disease. However, patency loss occurs in ≥10% of patients within 12 months posttreatment with poor understanding of the underlying mechanisms.

Objectives: The authors sought to investigate the determinants of DCB failure in femoropopliteal disease.

Methods: Data from randomized clinical trials (IN.PACT SFA, MDT-2113 SFA Japan) and 2 prespecified imaging cohorts of the IN.PACT Global Clinical Study were included. Influential procedural characteristics were evaluated by an independent angiographic core laboratory. The primary endpoint was DCB failure (patency loss during follow-up). Additional endpoints were binary restenosis and clinically driven target lesion revascularization. Multivariable analyses evaluated the clinical, anatomical, and procedural predictors of DCB failure.

Results: Included were 557 participants with single lesions and 12-month core laboratory-adjudicated duplex ultrasonography. Key clinical characteristics were as follows: mean age 68.8 years, 67.5% male, 87.6% with hypertension, 76.9% with hyperlipidemia, 40.5% with diabetes mellitus, 90.5% in Rutherford Classification Category (RCC) 2 to 3, and 9.5% in RCC 4 to 5. Average length and reference vessel diameter (RVD) were 16.37 cm and 4.66 mm, respectively; 49.7% of lesions were totally occluded. In multivariable analysis, only residual stenosis >30% was associated with patency loss, whereas residual stenosis >30% and smaller preprocedure RVD were associated with increased binary restenosis risk. RCC >3 and residual stenosis >30% were associated with increased 12-month clinically driven target lesion revascularization risk.

Conclusions: Patency loss after DCB treatment was influenced by procedural and clinical factors. Residual stenosis >30%, smaller preprocedure RVD, and higher RCC may be considered predictors of increased risk of DCB failure and its components in femoropopliteal artery disease.

Comments: Although bypass surgery was formerly the only therapeutic option for symptomatic lower limb peripheral arterial disease (PAD), endovascular revascularization has become the dominant therapy. So, modern endovascular treatment for PAD involving the femoro-popliteal segment (FPS) encompasses a variety of techniques ranging from atherectomy to the use of scaffolds to enhance blood flow through the treated segments. The usage of drug-coated balloons in this setting is fast expanding because they outperform noncoated percutaneous transluminal angioplasty for up to 5 years. However, with DCB, patency loss occurred in 10% of patients within 12 months of the procedure. Furthermore, the underlying mechanisms are poorly understood. This has been addressed by this JACC article.

The authors here sought to investigate the determinants of the DCB failure in PAD. Data from randomized clinical trials (IN.PACT SFA, MDT-2113 SFA Japan) and 2 prespecified imaging cohorts of the IN.PACT Global Clinical Study were included in this study. The scope of the study was quite large and data was collected from 83 centers in 17 countries. DCB failure was the major endpoint (patency loss during follow-up). Binary restenosis and clinically guided target lesion revascularization were additional endpoints. The clinical, anatomical, and procedural determinants of DCB failure were studied using multivariable analysis. The clinical, anatomical, and procedural determinants of DCB failure were studied using multivariable analysis.
Observations

| Conditions                                      | Outcomes                                                                 |
|------------------------------------------------|--------------------------------------------------------------------------|
| 1 DCB failure patients                         | patency loss was 17%, binary restenosis 15% and clinically driven target vessel revascularisation 5% |
| 2 Residual angiographic stenosis of more than 30% | Independently predicted loss of patency                                  |
| 3 Residual angiographic stenosis of more than 30% and smaller preprocedure reference vessel diameter (RVD) | Associated with increased binary restenosis risk                        |
| 4 Residual angiographic stenosis of more than 30% and RCC >3 | Associated with increased 12-month clinically driven target lesion revascularization risk. |

Strengths

The key finding in the study is very clinically relevant because it highlights factors that are early markers for potential DCB failure. The successful usage of DCB during the procedure can affect the quality of life of the patients, including improved symptoms and long-term patency of the vessel along with aggressive guideline-directed medical therapy for PAD.

Future Scope

Future studies should include usage of technologies like IVUS or OCT that will reduce the underestimation of the residual stenosis following DCB usage. Further studies involving balloon material and drug coating like paclitaxel are required to further improve the outcomes.

Take Home Message

A single factor, that is, the presence of residual angiographic stenosis of more than 30% postprocedure, fairly predicts the DCB outcomes.

Percutaneous Revascularization for Ischemic Left Ventricular Dysfunction (REVIVED-BCIS2)

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Abstract

Background: Whether revascularization by percutaneous coronary intervention (PCI) can improve event-free survival and left ventricular function in patients with severe ischemic left ventricular systolic dysfunction, as compared with optimal medical therapy (i.e., individually adjusted pharmacologic and device therapy for heart failure) alone, is unknown.

Methods: We randomly assigned patients with a left ventricular ejection fraction of 35% or less, extensive coronary artery disease amenable to PCI, and demonstrable myocardial viability to a strategy of either PCI plus optimal medical therapy (PCI group) or optimal medical therapy alone (optimal-medical-therapy group). The primary composite outcome was death from any cause or hospitalization for heart failure. Major secondary outcomes were left ventricular ejection fraction at 6 and 12 months and quality-of-life scores.

Results: A total of 700 patients underwent randomization—347 were assigned to the PCI group and 353 to the optimal-medical-therapy group. Over a median of 41 months, a primary-outcome event occurred in 129 patients (37.2%) in the PCI group and in 134 patients (38.0%) in the optimal-medical-therapy group (hazard ratio, 0.99; 95% confidence interval [CI], 0.78 to 1.27; P = .96). The left ventricular ejection fraction was similar in the 2 groups at 6 months (mean difference, −1.6 percentage points; 95% CI, −3.7 to 0.5) and at 12 months (mean difference, 0.9 percentage points; 95% CI, −1.7 to 3.4). Quality-of-life scores at 6 and 12 months appeared to favor the PCI group, but the difference had diminished at 24 months.

Conclusions: Among patients with severe ischemic left ventricular systolic dysfunction who received optimal medical therapy, revascularization by PCI did not result in a lower incidence of death from any cause or hospitalization for heart failure. (Funded by the National Institute for Health and Care Research Health Technology Assessment Program; REVIVED-BCIS2 ClinicalTrials.gov number, NCT01920048. opens in new tab.)

Comments: There is less clarity on the effectiveness and exact role of PCI in extensive CAD patients with severe LV systolic dysfunction. Even though there is a long-held belief among cardiologists that there may not be much benefit in performing angioplasty for patients with severe LV systolic dysfunction unless we show viability in the concerned territory. This study included patients with severe LV systolic dysfunction with an ejection fraction of less than 35% with extensive CAD classified with a BCIS jeopardy score of 6. The third criterion was to show the viability of at least 4
segments on cMRI/DSE or SPECT/PET. Patients had stable CAD and compensated HF. About 700 subjects were randomly assigned into PCI and OMT groups with follow-up for 2 years.

Primary outcomes of the study showed no significant improvement in all-cause mortality with PCI vs OMT as 37.2% vs 38% (P = .99). This was in agreement with the STITCH trial. The overall improvement in the OMT will improve the mortality percentage in the future, but the primary problem of extensive CAD and weak hearts will remain.

**Strengths:** The study had a mean LVEF of 27%, which followed the study criterion. The median BCIS score was 10, and about 100 patients had left the main disease. Almost all the patients were on optimal medical therapy, including a quarter of them on various cardiac devices. There was no mortality benefit, but there was definite but transient symptomatic improvement. So, there was improvement in the general well-being of the patients. “Transient” because I assume the newer drugs like SGLT2 and ARNI, which were included during the study, improved the OMT outcomes, thus improving the KCCQ scores later in the study.

**Limitations:** The Stitch trial showed that the viability of LV areas had no association with the outcomes in the postrevascularization group, but this study included viability as the third criterion to include the patients in the trial. A possible explanation could be the differentiation of the patients between viability and nonviability areas, which in turn could guide the operator to choose the possible artery for intervention. Also, it is assumed that the nonviable territory will not benefit from revascularization. When compared to previous trials, this study included a comparatively older population (about half of the population was over 70 years old). Cardiovascular mortality was not included in the primary outcome.

**Long-Term Efficacy and Safety of Renal Denervation in the Presence of Antihypertensive drugs (SPYRAL HTN-ON MED): A Randomized, Sham-Controlled Trial**

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**Abstract**

**Background:** Renal denervation has been shown to lower blood pressure in the presence of antihypertensive medications; however, long-term safety and efficacy data from randomized trials of renal denervation are lacking. In this prespecified analysis of the SPYRAL HTN-ON MED study, we compared changes in blood pressure, antihypertensive drug use, and safety up to 36 months in renal denervation versus a sham control group.

**Methods:** This randomized, single-blind, sham-controlled trial enrolled patients from 25 clinical centers in the USA, Germany, Japan, the UK, Australia, Austria, and Greece, with uncontrolled hypertension and office systolic blood pressure between 150 mm Hg and 180 mm Hg and diastolic blood pressure of 90 mm Hg or higher. Eligible patients had to have 24-h ambulatory systolic blood pressure between 140 mm Hg and less than 170 mm Hg, while taking 1 to 3 antihypertensive drugs with stable doses for at least 6 weeks. Patients underwent renal angiography and were randomly assigned (1:1) to radiofrequency renal denervation or a sham control procedure. Patients and physicians were unmasked after 12-month follow-up and sham control patients could cross over after 12-month follow-up completion. The primary endpoint was the treatment difference in mean 24-h systolic blood pressure at 6 months between the renal denervation group and the sham control group. Statistical analyses were done on the intention-to-treat population. Long-term efficacy was assessed using ambulatory and office blood pressure measurements up to 36 months. Drug surveillance was used to assess medication use. Safety events were assessed up to 36 months. This trial is registered with ClinicalTrials.gov, NCT02439775; prospectively, an additional 260 patients are currently being randomly assigned as part of the SPYRAL HTN-ON MED Expansion trial.

**Findings:** Between July 22, 2015 and June 14, 2017, among 467 enrolled patients, 80 patients fulfilled the qualifying criteria and were randomly assigned to undergo renal denervation (n = 38) or a sham control procedure (n = 42). Mean ambulatory systolic and diastolic blood pressure were significantly reduced from baseline in the renal denervation group, and were significantly lower than the sham control group at 24 and 36 months, despite a similar treatment intensity of antihypertensive drugs. The medication burden at 36 months was 2.13 medications (SD 1.15) in the renal denervation group and 2.55 medications (2.19) in the sham control group (P = .26). A total of 24 (77%) of 31 patients in the renal denervation group and 25 (93%) of 27 patients in the sham control group adhered to medication at 36 months. At 36 months, the ambulatory systolic blood pressure reduction was −18.7 mm Hg (SD 12.4) for the renal denervation group (n = 30) and −8·6 mm Hg (14.6) for the sham control group (n = 38). P = .0055) for mean ambulatory diastolic blood pressure, −11.0 mm Hg (−19.8 to −2.1; P = .016) for morning systolic blood pressure, and −1.8 mm Hg (−19.0 to −4.7; P = .0017) for night-time systolic blood pressure. There were no short-term or long-term safety issues associated with renal denervation.
Interpretation

Radiofrequency renal denervation compared with sham control produced a clinically meaningful and lasting blood pressure reduction up to 36 months of follow-up, independent of concomitant antihypertensive medications and without major safety events. Renal denervation could provide an adjunctive treatment modality in the management of patients with hypertension.

Comments

Hypertension is the leading cause of mortality worldwide. Because of poor adherence to oral therapy, alternative modes of management are being explored to get sustained BP control with less drug burden. The RF catheter-based renal denervation (RDN) technique is safe and has been shown to be effective in controlling BP in multiple studies. But we lack long-term studies to show the effectiveness of this technique. This study by Mahfoud et al published in April 2022, showed a 3-year follow-up data on RDN compared to sham-controlled trials.

Some significant findings to be noted are as follows: the average age of both groups (RDN vs Sham) was similar at 53.9 8.9 vs 53.0 10.7 with males contributing up to 87% vs 81% of the total subjects, 38 vs 42. No other significant differences in comorbidities were noted. Subjects with isolated systolic hypertension were excluded. The average systolic and diastolic BP among the groups was similar at the beginning and post procedure, a 36-month follow-up was carried out. At the end of 36 months, there was a significant reduction in the BP readings in the RDN group compared to the Sham group. The average difference in treated BP readings at the end of 36 months was 10 mm Hg for SBP and 5.9 mm Hg for DBP. This also reduced the drug burden in the RDN group compared to the sham group.

Strengths: This study was multicentric, randomized, and blinded. This study highlights that the long-term effects of the RDN persist and become more prominent as time passes. RDN demonstrates an “always on” effect with sustained BP reduction throughout the day and night during 24-h ambulatory BP (RDN: 83.3% vs. Sham: 43.8% of subjects had SBP 140 mmHg/24 h). There were no causes of death in the RDN group and 1 in the Sham group.

Limitations: This study was privately funded by Medtronic, Inc. During the COVID-19 pandemic, BP control may have worsened in spite of the “in-person follow-up” performed as claimed by the study group. Another important history not recorded was exercise and diet during these 36 months, which could have impacted the results. In spite of these short-comings, the study directs us toward the safety and effectiveness of the RDN for persistent high BP.

The FRAME-AMI Trial—FFR vs. Angiography-Guided PCI in AMI With Multivessel Disease

Session: HOT LINE SESSION 7 [ESC 2022]
Topic: Primary Percutaneous Coronary Intervention (PCI)
Speaker: Dr J. Hahn (Seoul, KR)
https://esc365.escardio.org/presentation/255332?resource=slide

August 28, 2022

FRAME-AMI was an investigator-initiated, open-label trial conducted at 14 sites in Korea. The trial randomly assigned patients with acute myocardial infarction and multivessel coronary artery disease who had undergone successful PCI of the IRA to undergo either (1) FFR-guided PCI of non-IRA with FFR ≤0.80 or (2) angiography-guided PCI of non-IRA with >50% diameter stenosis. In both groups, complete revascularization during the index procedure was recommended. However, staged procedures during the index hospitalization were permitted at operators’ discretion. The primary endpoint was a composite of all-cause death, myocardial infarction, or repeat revascularization.

Between August 2016 and December 2020, a total of 562 patients underwent randomization. The average age was 63 years and 16% were women. Non-IRA lesions were treated by immediate PCI after successful treatment of IRA in 337 patients (60.0%) and by staged procedure during the same hospitalization in 225 patients (40.0%). During a median follow-up of 3.5 years (interquartile range 2.7-4.1 years), the primary endpoint occurred in 18 of 284 patients in the FFR group and 40 of 278 patients in the angiography group (Kaplan-Meier event rates at 4 years, 7.4% versus 19.7%; hazard ratio [HR] 0.43; 95% confidence interval [CI] 0.25-0.75; P = .003).

The incidence of death was significantly lower in the FFR group compared with the angiography group, occurring in 5 patients versus 16 patients, respectively (Kaplan-Meier event rates at 4 years, 2.1% versus 8.5%; HR 0.30; 95% CI 0.11-0.83; P = .020). The incidence of myocardial infarction was also significantly lower in the FFR group compared with the angiography group, occurring in 7 patients versus 21 patients, respectively (Kaplan-Meier event rates at 4 years, 2.5% versus 8.9%; HR 0.32; 95% CI 0.13-0.75; P = .009). Ten patients in the FFR group had an unplanned revascularization compared with 16 patients in the angiography group, with no significant difference between the 2 groups (Kaplan-Meier event rates at 4 years, 4.3% versus 9.0%; HR 0.61; 95% CI 0.28-1.34; P = .216).
Comments

There is a growing body of data and evidence that the use of FFR is associated with better patient outcomes and long-term benefits. A study of selective PCI of non-infarct-related artery (IRA) lesions using FFR guided decision-making in patients with acute myocardial infarction (AMI) and multivessel disease when compared to routine PCI based on angiographic diameter stenosis [FRAME-AMI trial] was presented on August 28 during ESC Congress 2022 in Barcelona.

We have seen that multiple RCTs have consistently found that PCI of non-IRA lesions for complete revascularization in patients with ST-segment elevation myocardial infarction (STEMI) improves clinical outcomes compared with IRA-only PCI. ESC guidelines recommend that revascularization of non-IRA lesions should be considered in STEMI patients with multivessel disease during the index procedure or before hospital discharge in a staged manner. However, the optimal strategy to select targets for non-IRA PCI has not been clarified in these guidelines. In this context, the FRAME-AMI trial fits in and gives information about FFR-guided PCI vs. angiography-guided PCI for non-IRA lesions in patients with acute MI and multivessel disease.

This trial randomized 563 patients with AMI and non-IRA lesions from 14 sites in Korea to PCI with either FFR or angiography. Patients with non-IRA lesions with an FFR of 0.80 or lower were treated with PCI (n = 284) in the FFR group, while patients with non-IRA lesions with a diameter stenosis of >50% on visual estimation were treated with PCI in the angiography group (n = 278). The primary endpoint was a composite of all-cause death, MI, or unplanned revascularization. The median follow-up was 3.5 years.

According to the trial investigators, non-IRA lesions were treated by immediate PCI after successful treatment of IRA in 337 patients (60.0%) and by staged procedure during the same hospitalization in 225 patients (40.0%). The primary endpoint occurred in 18 patients (7.4%) in the FFR group and 40 patients (19.7%) in the angiography group. The incidence of both death and MI was significantly lower in the FFR group compared with the angiography group (5 vs. 16 patients and 7 vs. 21, respectively). Additionally, 10 patients in the FFR group had an unplanned revascularization compared with 16 patients in the angiography group, with no significant difference between the two groups.

Benefits: The efficacy of FFR-guided PCI on the primary endpoint was consistent regardless of STEMI or non-STEMI. This trial was a multicentric RCT and had a good follow-up period.

This study was not powered enough to change the guidelines, but this study can provide the data to consider FFR in non-IRA lesions for decision-making.

Trans-Radial Approach Versus Trans-Femoral Approach in Patients With Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention: An Updated Meta-Analysis of Randomized Controlled Trials

Senguttuvan NB, Reddy PMK, Shankar P, Abdulkader RS, Yallanki HP, Kumar A, et al.
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Abstract

Introduction: Trans-radial approach (TRA) is recommended over trans-femoral approach (TFA) in patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI). We intended to study the effect of access on all-cause mortality.

Methods and Results: We searched PubMed and EMBASE for randomized studies on patients with ACS undergoing PCI. The primary outcome was all-cause mortality at 30 days. The secondary outcomes included in-hospital mortality, major adverse cardiac or cerebrovascular event (MACE) as defined by the study, net adverse clinical event (NACE), nonfatal myocardial infarction, nonfatal stroke, stent thrombosis, study-defined major bleeding, and minor bleeding, vascular complications, hematoma, pseudoaneurysm, nonaccess site bleeding, need for transfusion, access site cross-over, contrast volume, procedure duration, and hospital stay duration. We studied 20,122 ACS patients, including 10,037 and 10,085 patients undergoing trans-radial and trans-femoral approaches, respectively. We found mortality benefit in patients with ACS for the trans-radial approach (1.7% vs 2.3%; RR: 0.75; 95% CI: 0.62-0.91; P = 0.004; I2 = 0%). Out of 10,465 patients with STEMI, 5,189 patients had TRA and 5,276 had TFA procedures. A similar benefit was observed in patients with STEMI alone (2.3% vs. 3.3%; RR: 0.71; 95% CI: 0.56-0.90; P = 0.004; I2 = 0%). We observed reduced MACE, NACE, major bleeding, vascular complications, and pseudoaneurysms. No difference in re-infarction, stroke, and serious bleeding requiring blood transfusions was noted. We noticed a small decrease in contrast
volume (mL) (mean difference [95% CI]: −4.6 [−8.5 to −0.7]), small but significantly increase in procedural time (mean difference [95% CI] 1.2 [0.1 to 2.3]), and fluoroscopy time (mean difference [95% CI] 0.8 [0.3 to 1.4] min) in the transradial group.

**Conclusion:** TRA has significantly reduced 30-day all-cause mortality among patients undergoing PCI for ACS. TRA should be the preferred vascular access in patients with ACS.

**Comments:** The European Society of Cardiology (ESC) has announced the presentation of data from a Radial Trialists’ Collaboration (RTC) study, which shows that radial artery access for coronary angiography or percutaneous coronary intervention (PCI) is associated with lower risks of all-cause death and bleeding when compared to femoral access. The late-breaking research was presented in a Hot Line session at the 2022 ESC Congress held from August 26 to 29 in Barcelona, Spain.

In patients requiring coronary catheterization, both European and American guidelines recommend a trans-radial approach (TRA) over a transfemoral approach (TFA). When compared to TFA, TRA has a lower incidence of access site-related bleeding and vascular complications. In previous studies, TRA was associated with a mortality benefit; however, none of the analyses were adequately powered for individual endpoints, including mortality. This study provides adequate power and strong evidence from a multi-centric randomized trial comparing radial vs femoral access for PCI. This study showed reduced all-cause mortality. The benefit begins soon after PCI (ie, within 10 days) and continues for up to 30 days.

The meta-analysis incorporated data from 7 trials, totaling 21,600 patients. Of these, 10,775 were randomly assigned to TRA and 10,825 to TFA. The median age of the patients was 63.9 years. A total of 31.9% were female, 95% had acute coronary syndrome, and 75.2% had PCI. The primary outcome of the study was 30-day all-cause mortality, and the coprimary outcome was 30-day major bleeding. The primary analysis was carried out using an intention-to-treat cohort. The TRA group had a lower incidence of all-cause death than the TFA group (1.5% vs 2.7%) (odds ratio, 0.63-0.95; 95% CI, 0.63-0.95; \( P = .012 \)). Major bleeding was also significantly reduced with TRA versus TFA (1.5% vs 2.7%) (odds ratio, 0.55; 95% CI, 0.45-0.67; \( P = .001 \)).

The survival benefit was confirmed in the per-protocol, as-treated, PCI, acute coronary syndrome, and myocardial infarction cohorts. The effects of TRA were also consistent across the majority of prespecified subgroups, and the findings indicated that patients with baseline anemia might have a greater mortality benefit compared to those without anemia. Additionally, the investigators reported that in a multivariable model, TRA was independently associated with a significant 24% relative risk reduction of 30-day all-cause mortality and a 51% reduction of major bleeding. Mediation analysis showed that stopping major bleeding didn’t have much of an effect on the effect of TRA on death.

It should be noted that the benefits of TRA for mortality, major bleeding, and other clinical outcomes apply primarily to patients with acute coronary syndrome, who made up approximately 95% of the study population, and should not be fully extended to elective patients undergoing coronary angiography with or without PCI. This study establishes TRA as the gold standard for patients undergoing cardiac catheterization with or without PCI, thereby supporting the "radial-first" approach.

### Pragmatic Trial Comparing Symptom-Oriented Versus Routine Stress Testing in High-Risk Patients Undergoing Percutaneous Coronary Intervention—POST-PCI

**Anthony A Bavry**

Date Presented: 08/28/2022

[https://www.acc.org/Latest-in-Cardiology/Clinical-Trials/2022/08/27/04/13/POST-PCI](https://www.acc.org/Latest-in-Cardiology/Clinical-Trials/2022/08/27/04/13/POST-PCI)

**Aim of the Study**

To find whether routine functional testing at 12 months post PCI was beneficial among high-risk patients who underwent PCI.

Patients who underwent PCI and had high-risk clinical or anatomical characteristics were randomized to functional testing \( n = 849 \) versus standard of care \( n = 857 \). In the functional testing group, subjects could undergo nuclear stress testing or stress echocardiography at 12 months. Exercise electrocardiography was permissible but discouraged due to high rate of false-positive results.

| Total number of enrollees: 1,706 | Inclusion criteria: Patients who underwent PCI and had high-risk clinical or anatomical characteristics. High-risk **anatomical** characteristics included left main disease, bifurcation disease, ostial lesion, chronic total occlusion, multivessel PCI, re-stenotic lesion, diffuse lesion (ie, stent length >32 mm) High-risk **clinical** characteristics included diabetes mellitus, chronic renal failure (serum creatinine level ≥2.0 mg/dL or hemodialysis), and acute coronary syndrome |
| --- | --- |
| Duration of follow-up: 24 months | Exclusion criteria: Cardiogenic shock Treated with bare-metal stents or balloon angioplasty alone Pregnancy Limited life expectancy Participation in another investigational study |
| Mean patient age: 65 years | Percentage female: 22% Percentage with diabetes: 39% |
Principal Findings
The primary outcome, all-cause mortality, myocardial infarction, or hospitalization for unstable angina at 2 years, occurred in 5.5% of the functional testing group compared with 6.0% of the standard care group (P = .62).

Secondary Outcomes
Invasive coronary angiography at 2 years: 12.3% of the functional testing group compared with 9.3% of the standard care group (P = .62). Repeat revascularization at 2 years: 8.1% of the functional testing group compared with 5.8% of the standard care group (P = not significant).

Comments
This study established no role for routine functional testing at 12 months post-high risk PCI. Routine functional testing was associated with a numerical increase in invasive coronary angiography and repeat revascularization at 24 months. However, this did not reduce the incidence of adverse cardiovascular events. Also, at 2 years, there was no difference in the composite outcome of death from any cause, myocardial infarction (MI), or hospitalization for unstable angina between patients who had routine functional testing at 1 year and patients receiving standard care in POST-PCI.

This compelling new evidence by the “POST-PCI trial” failed to show that routine functional testing after PCI prevents adverse cardiovascular events. This was in line with an earlier study, the “Ischemia Trial,” where the concept of “less intervention is more beneficial” was established. Despite the fact that the patients in these trials had very different characteristics, a more invasive therapeutic approach (in the ISCHEMIA trial) and a more aggressive follow-up approach (in the POST-PCI trial) did not provide an additional treatment benefit over conservative management based on guideline-directed medical therapy.

While routine functional testing is common among patients with coronary artery disease, this practice is not recommended. The POST-PCI trial adds compelling new evidence to support a future class III recommendation for routine post-PCI surveillance testing. Until then, in the absence of other clinical signs or symptoms suggestive of stent failure, we must refrain from prescribing surveillance stress testing to our patients following PCI.

Ultrasound-Assisted Catheter-Directed Thrombolysis Versus Anticoagulation Alone for Management of Submassive Pulmonary Embolism

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Background: Patients with submassive pulmonary embolism (PE) are vulnerable to sudden deterioration, recurrent PE, and progression to pulmonary hypertension and chronic right ventricular (RV) dysfunction. Previous studies have suggested a clinical benefit of using ultrasound-assisted catheter-directed thrombolysis (USCDT) to invasively manage patients with submassive PE. However, there is sparse data comparing the clinical outcomes of these patients when treated with USCDT versus anticoagulation (AC) alone. We sought to compare the outcomes of USCDT versus AC alone in the management of submassive PE.

Methods: A total of 192 consecutive patients who underwent USCDT for submassive PE between January 2013 and February 2019 were identified. ICD9/ICD10 codes were used to detect 2,554 patients diagnosed with PE who did not undergo thrombolysis. Propensity matching identified 192 patients with acute PE treated with AC alone. Clinical outcomes were compared between the 2 groups. Baseline demographics, laboratory values, and pulmonary embolism severity index scores were similar between the 2 cohorts.

Results: There was a significant reduction in mean systolic pulmonary artery pressure (sPAP) in the USCDT group compared to the AC group (A11 vs A3.9 mmHg, P < .001). There was significant improvement in proportion of RV dysfunction in all patients, but the difference was larger in the USCDT group (Δ43.3% vs Δ17.3%, P < .001). Patients who underwent USCDT had lower 30-day (4.3% vs 10.5%, P = .03), 90-day (5.5% vs 12.4%, P = .03), and 1-year mortality (6.2% vs 14.2%, P = .03).

Conclusions: In patients with acute submassive PE, USCDT was associated with improved 30-day, 90-day, and 1 year mortality as compared to AC alone. USCDT also improved RV function and reduced sPAP to a greater degree than AC alone. Further studies are needed to verify these results in both short- and long-term outcomes.

Comments: According to the 2011 AHA guidelines, “submassive” pulmonary thromboembolism (PTE) is defined as those patients with acute PE without systemic hypotension but with evidence of either right ventricle (RV) dysfunction or myocardial necrosis. Pulmonary embolism (PE) is a leading cause of morbidity and mortality, with considerable diagnostic and treatment problems. Clinical manifestations range from mild, nonspecific symptoms to syncope, shock, and death. Patients who have hemodynamic instability and/or symptoms of right ventricular dysfunction are at a greater risk of negative outcomes and may benefit from aggressive therapy and care. In the absence of contraindications, therapeutic anticoagulation is recommended for all patients. Thrombolysis, either by systemic infusion or percutaneous catheter-directed therapy, should be seriously explored in selected high- and intermediate-risk patients. For individuals who fail or cannot tolerate anticoagulation and/or thrombolysis, other treatment methods, including vena cava filters and surgical embolectomy, are available.

Previous research has revealed that employing ultrasound-assisted catheter-directed thrombolysis (USCDT) to address patients with submassive PE has a therapeutic advantage. However, data on the clinical outcomes of these individuals
when treated with USCDT versus anticoagulation (AC) alone is limited. The authors sought to see how USCDT fared when compared to AC alone in the treatment of submassive PE.

In this study, 193 patients who underwent USCDT were compared with 192 patients who were treated with AC alone. The results included significant improvement in systolic pulmonary artery pressure in the USCDT vs AC groups. RV function improved in 43.3% of the USCDT group versus 17.3% in the AC group. Also, there was overall low mortality in USCDT vs. AC groups.

**Strengths:** This study is one of the few large studies comparing USCDT and AC groups. This study had good follow-up with up to 1-year follow-up, giving a fairer idea as to the overall long-term response to USCDT.

No randomization was done. It is a single-center study. Further large and robust studies are required to reaffirm the above outcomes.

Randomized Trial of Left Bundle Branch vs Biventricular Pacing for Cardiac Resynchronization Therapy

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**Abstract**

**Background:** Left bundle branch pacing (LBBP) is the most rapidly growing conduction system pacing technique that is capable of correcting intrinsic left bundle branch block (LBBB). As such, it is potentially an optimal alternative to cardiac resynchronization therapy (CRT) with biventricular pacing (BiVP).

**Objectives:** The authors sought to compare the efficacy of LBBP-CRT with BiVP-CRT in patients with heart failure and reduced left ventricular ejection fraction (LVEF).

**Methods:** This is a prospective, randomized trial of patients with nonischemic cardiomyopathy and LBBB with 6-month preplanned follow-up. Crossovers were allowed if LBBP or BiVP were unsuccessful. The primary endpoint was the difference in LVEF improvement between 2 groups. The secondary endpoints included changes in echocardiographic measurements, N-terminal pro-B-type natriuretic peptide (NT-proBNP), New York Heart Association functional class, 6-minute walk test, QRS duration, and CRT response.

**Results:** The study included 40 consecutive patients (20 males, mean age 63.7 years, LVEF 29.7% ± 5.6%). Crossovers occurred in 10% of LBBP-CRT and 20% of BiVP-CRT. All patients completed follow-up. Intention-to-treat analysis showed significantly higher LVEF improvement at 6 months after LBBP-CRT than BiVP-CRT (mean difference: 5.6%; 95% CI: 0.3-10.9; *P* = .039). LBBP-CRT also appeared to have greater reductions in left ventricular end-systolic volume (−24.97 mL; 95% CI: −49.58 to −0.36 mL) and NT-proBNP (−1,071.80 pg/mL; 95% CI: −2,099.40 to −44.20 pg/mL), and comparable changes in New York Heart Association functional class, 6-minute walk distance, QRS duration, and rates of CRT response compared with BiVP-CRT.

**Conclusions:** LBBP-CRT demonstrated greater LVEF improvement than BiVP-CRT in heart failure patients with nonischemic cardiomyopathy and LBBB.

**Comments:** Up to 30% of patients with moderate-to-severe LV dysfunction have underlying bundle branch obstruction and electromechanical dyssynchrony. Cardiac resynchronization therapy (CRT) with biventricular pacing has remained the preferred therapy. However, biventricular pacing is underutilized, and nonresponse is observed in 13 to 15% of cases. The question is, why?

By biventricular pacing by CRT, we mean nonphysiological electrical resynchronization between the epicardium from the coronary sinus lead and the right ventricular endocardium. Second, it's not uncommon to hear that differences in the way a person's body is built can cause a lead to be placed in a less-than-ideal spot or cause a coronary sinus lead placement to fail. We also face high-pacing thresholds and fragmented lead stimulation. So, the question raised at multiple forums was, do we have a better way of pacing? Well, we have hss bundle pacing, but it has failed to show any clear advantages over biventricular pacing. So, the next candidate to consider is bundle branch pacing. Left bundle branch pacing (LBBP) was first described and performed by Huang et al in 2017. As a result, data from case reports and short observational studies indicates that LBBP is a promising strategy for providing physiological pacing. However, these findings were hampered by a relatively short follow-up period, a lack of prospective enrolment, and in many cases, LBB capture was not adequately defined, so some patients may not have had conduction system capture. To some extent, this study tried to address

Here, the authors sought to compare the efficacy of LBBP-CRT with BiVP-CRT in patients with heart failure and reduced left ventricular ejection fraction (LVEF) with LBBB. A cross over was allowed if the LBBP proved to be a failure. The primary end point was to check for improvement in LVEF between the two groups. Secondary end points included echocardiography changes, NT-Pro BNP levels, NYHA classification, 6-minute walk test, QRS duration, and CRT response. This included 40 patients, 20 males and 20 females, with a mean age of 63 years and a mean LVEF of 29%.

**Result**

1. All patients completed the follow-up, and significant improvement in LVEF after 6 months of post LBBP when compared to BiVP-CRT. The mean difference in ejection fraction was 5.6%.
2. LBBP-CRT also to appears to have higher reduction of LV-ESV and decrease in NT-Pro BNP.
In the end, LBBP-CRT improved LVEF more than BiVP-CRT in patients with heart failure who had nonischemic cardiomyopathy and LBBB.

**Strengths:** This is a prospective randomized trial. This is the first head-to-head RCT comparing LBBP-CRT vs BiVP-CRT among LBBB with low LVEF patients. This study might form the basis for a more robust RCT study in the future. The LBBP is being received more enthusiastically by the EP specialists.

**Challenges:** Even though LBBP-CRT appears to be a safe and effective way of achieving electromechanical resynchronization, heart failure patients who present to the clinic or ER are a heterogenous group. The majority may present with ischemic cardiomyopathy or multiple other comorbidities.

As of now, we can reserve LBBP-CRT for nonischemic cardiomyopathy with LBBB or focal LBBB. More complex conduction defects may be addressed by combining Hiss bundle pacing or coronary sinus pacing with LBBP.

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