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LETTER TO THE EDITOR

# Cost-effectiveness of radial vs. femoral approach in primary percutaneous coronary intervention in STEMI – Randomized, control trial

**KEYWORDS**
acute coronary syndrome (ACS);
costs;
primary percutaneous coronary intervention (PCI)

**Abstract** *Introduction and objectives:* Primary percutaneous coronary intervention infarction became the preferred method of treatment for myocardial ST segment elevation. Improved safety was reported in transradial access (radial) compared to transfemoral access (femoral). The aim of this study was to compare the cost between the two access points in ST segment elevation myocardial infarction.
*Methods:* This is a subanalysis of the OCEAN RACE trial in which 103 myocardial infarction patients were randomized to either the radial (n=52) or femoral (n=51) groups. The clinical safety and efficacy were recorded during the hospital stay. The procedural metrics were meticulously logged, and costs were evaluated using the micro-cost method. The indirect costs were estimated using the human capital approach.
*Results:* Clinical success was numerically higher in the radial group (90.4 vs. 80.4%, p=0.123). There were no differences in major adverse cardiac events (9.6% vs. 11.8%, p=0.48) and death (2.0% vs. 6.0%, p=0.31). The average in-hospital cost per patient was 2,740 ± 1,092 EUR. The cost of therapeutic success was lower in the radial group at 3,060 EUR vs. 3,374 EUR. The indirect costs related to absence at work were 138 EUR per patient, which were lower in the radial group compared to the femoral group.
*Conclusions:* The total in-hospital costs were similar between the study groups. The indirect costs were lower in the radial group. Introduction of radial access as the default approach in all centers may significantly reduce the overall financial burden from a social perspective.


## 1. Introduction

The primary percutaneous coronary intervention (PCI) in ST segment elevation myocardial infarction (STEMI) accounted for 36% (n=28,278) of all interventions in acute coronary syndrome in Poland in the year 2012.[1] The transradial (TR) approach became a default strategy for many independent operators in Poland, which is consistent with current European Society of Cardiology recommendations.[2] Improved safety of TR procedures compared to transfemoral (TF) was demonstrated.[3] The first feasibility reports emerged in the 90s and TR was used in selected patients with extensive aorto-iliac disease, severe tortuosity of the aorta or other anatomical contraindications for TF access.[4] The radial artery, unlike the femoral or brachial artery, is not an end-artery. Therefore, even when the radial artery is occluded, adequate ulnar artery collaterals can salvage the hand from ischemia. It is an easy artery to compress and sheath removal results in diminished risk of bleeding and other vascular complications.[5] Yet, the smaller radial artery size, weaker pulse and more tortuosity may contribute to increased procedural metrics, including time in the cath

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**List of abbreviations**

| | |
|---|---|
| 95% CI | 95% confidence interval |
| OCEAN RACE | Access for percutaneous coronary intervention in STEMI: radial vs. femoral - prospective, randomized clinical trial |
| PCI | percutaneous coronary intervention |
| STEMI | ST segment elevation myocardial infarction |
| TF | transfemoral |
| TR | transradial |

lab, contrast volume and radiation exposure. The decision regarding transition of the entire spectrum of interventions towards a TR strategy must take into consideration the economic burden from local and social perspectives as well. In patients undergoing diagnostic catheterization or elective PCI there is a cost-benefit for TR access.[6] Whether the cost-effectiveness is also true for TR in primary PCI in STEMI patients has not been demonstrated yet.

The aim of this study was to assess costs and cost-effectiveness of TR compared to TF access in a STEMI population treated with primary PCI. To study this procedure, we designed a prospective randomized controlled trial with a predefined economic study protocol. The clinical results of the "Access for percutaneous coronary intervention in STEMI: radial vs. femoral - prospective, randomized clinical trial" (OCEAN RACE trial) have been published, and in this paper, we disclose the pharmacoeconomic subanalysis.[7]

## 2. Methods

The study population comprised 103 STEMI patients. A detailed description of the methodology and study flow were published with the clinical results of the OCEAN RACE trial.[7] In brief, the baseline characteristics of the two study groups are presented in Table 1. Patients were treated according to ESC STEMI guidelines.[8]

The cost-effectiveness analysis was performed from two perspectives: a hospital perspective with direct medical and nonmedical costs included and a societal perspective with indirect costs.

Clinical efficacy was defined in regard to angiographic success (a Thrombolysis in Myocardial Infarction flow of 3 and residual stenosis less than 20%) and clinical success (angiographic success, survival to hospital discharge, no major adverse cardiac events).

The following procedural metrics were recorded: angiography and angioplasty time, contrast volumes and materials used (including stents, balloons, wires, sterile gowns, local anesthetics and catheters for intra-aortic balloon pumps). The in-hospital time was calculated. Unplanned diagnostics, consultations and interventions driven by periprocedural complications were reported. We used the micro-cost method for collecting data on the resources that were utilized and the value of those resources. The indirect costs were estimated in regard to the patients' absence from work (absenteeism) by using the human capital approach. The value of the daily gross domestic product *per capita* (2012) was obtained from macroeconomic reports provided by the Polish Central Statistical Office.[9] All costs were reported in Polish zloty (PLN) and converted to EUR for the purpose of clarity. The conversion rate was 1 EUR = 4.24 Polish zloty.

In the cost-effectiveness analysis, we matched clinical efficacy with in-hospital costs and calculated the cost of therapeutic success (total cost/clinical efficacy) as well as the incremental cost-effectiveness ratio (Δ total cost/Δ clinical efficacy).

To understand how the choice of vascular access in STEMI patients may impact the national economy, we extrapolated the indirect costs onto the entire population by assuming that all primary PCI in STEMI were performed from TR access. The in-direct costs were calculated based on the daily value of gross domestic product *per capita*, which was multiplied by the average length of an in-hospital stay in each study arm. The difference was then presented as an in-direct cost benefit. All pharmacoeconomic analyses were performed with intention-to-treat results from RCT.

We used Student's t-test, the Kruskal-Wallis test, a chi-square test and Fisher's exact probability test to compare the TR arm vs. the TF arm. Data are presented as the mean values, median and hazard ratios with a 95% confidence interval (95% CI). P-values of less than 0.05 were considered to be statistically significant. The study was initiated and funded by investigators. The investigators followed the Consolidated Health Economic Evaluation Reporting Standards statement.[10]

## 3. Results

Patients were equally distributed in the study arms (TR:52/TF:51), and the baseline clinical characteristics did not differ between the groups. Angiographic success was achieved in 98.1% (TR) vs. 92.2% (TF) of cases, $p = 0.205$. In 99% of cases, the operator successfully crossed the occlusion with a guidewire and was able to achieve reperfusion. There were no differences between the groups in terms of the baseline Thrombolysis in Myocardial Infarction flow. Clinical success was achieved in 85.4% of cases and was numerically higher among individuals in the TR group (TR: 90.4 vs. 80.4%, $p = 0.123$). Clinical success was mainly driven by numerically higher angiographic success in the TR group, as reported previously. [7] The average in-hospital stay was 8.37 ± 5.77 days.

The average in-hospital cost per STEMI patient was 2,740 ± 1,092 EUR. The medical costs accounted for 85.5% of total costs (2,217±836 EUR). Overall, 52.7% of medical costs were associated with the Acute Coronary Unit and post-procedural pharmacotherapy (1,445±739 EUR). The procedural costs included diagnostic and angioplasty catheters, guidewires, balloons and stents, which comprised 21.2% of medical costs (581±338.5 EUR). There was a small cost difference in the total medical costs: 2,740 EUR in the TR group and 2,686.8 EUR in the TF group. The breakdown of costs is presented in Table 2.

The cost-effectiveness was analyzed in relation to in-hospital costs and clinical efficacy. The cost of clinical

**Table 1** Baseline clinical characteristics of patients on admission.

| | Radial access (n=52) | Femoral access (n=51) | p |
|---|---|---|---|
| Age — years | 61 (49.7—72.2) | 62.8 (50.2—75.4) | 0.44 |
| Height — cm | 170.4 (163.2—177.7) | 169.2 (159.9—178.5) | 0.48 |
| Weight — kg | 76 (60.5—91.5) | 77.8 (62.9—92.7) | 0.57 |
| BMI — kg/m$^2$ | 26 (21.7—30.2) | 27 (22.7—31.3) | 0.21 |
| BSA — m$^2$ | 1.89 (1.659—2.116) | 1.89 (1.674—2.104) | 0.95 |
| Pulse — bpm | 82 (60.8—103.0) | 78 (58.5—97.1) | 0.30 |
| Systolic blood pressure — mm Hg | 140.5 (110.2—170.8) | 132.2 (107.1—157.3) | 0.14 |
| Diastolic blood pressure — mm Hg | 77.5 (59.1—95.9) | 70.8 (55.8—85.9) | 0.05 |
| Hypertension | 69.8% | 68.2% | 1.00 |
| Diabetes type 2 | 18.2% | 27.7% | 0.33 |
| Previous MI | 7.7% | 8.3% | 1.00 |
| Hyperlipidemia | 69.2% | 75.0% | 0.66 |
| Chronic kidney disease | 12.0% | 18.4% | 0.41 |
| Peripheral artery disease | 13.2% | 15.4% | 1.00 |
| Smoking | 65.3% | 66.7% | 1.00 |
| Oral anticoagulation | 2.6% | 0.0% | 0.49 |
| Dysthyroidism | 10.0% | 12.5% | 1.00 |
| Carotid artery stenosis | 7.9% | 5.1% | 0.66 |
| Hemoglobin — g/dL | 13.7 (12.2—15.2) | 13.9 (12.5—15.3) | 0.45 |
| Platelets — 10$^3$/μl | 235.1 (169.2—301.0) | 226.5 (157.3—295.7) | 0.52 |
| Troponin — ng/ml | 6.5 (0.00—18.17) | 20.4 (0.00—77.28) | 0.09 |
| Creatinine — mg/dl | 1.0 (0.6—1.4) | 1.0 (0.6—1.4) | 0.46 |
| eGFR — mL/min./1.72 m$^2$ | 86.5 (62.4—110.6) | 87.9 (59.7—116.2) | 0.79 |
| Total cholesterol — mg/dL | 201 (153.3—248.7) | 197.6 (155.7—239.4) | 0.71 |
| LDL-C — mg/dL | 128.4 (89.4—167.4) | 121.9 (82.1—161.7) | 0.43 |
| HDL-C — mg/dL | 42.6 (26.7—58.5) | 44.4 (30.5—58.3) | 0.56 |
| Triglycerides — mg/dL | 169.3 (31.8—306.8) | 144.7 (70.1—219.3) | 0.28 |

Values are presented as averages (95% confidence interval) if not indicated otherwise; BMI - body mass index; BSA - body surface area; MI - myocardial infarction; eGFR - estimated glomerular filtration rate; LDL-C — low density lipoprotein cholesterol; high density lipoprotein cholesterol; HDL — high density lipoprotein cholesterol.

success was lower in the TR group (3,060 EUR vs. 3,374 EUR). The incremental cost-effectiveness ratio was 540 EUR per clinical success.

The average in-hospital expenditures related to complications included diagnosis and treatment costs. Both were relatively low and amounted to 3.9 EUR (TR: 2.7±14.6 EUR vs. TF: 5.1±20.7 EUR) and 50 EUR (TR: 48.0±27.8 EUR vs. TF: 52.4±47.6 EUR) per patient, respectively.

The value of the Polish annual gross domestic product during the study period was 363,019 × 10$^6$ EUR. The average daily value of gross domestic product *per capita* was 61.4 EUR. The average length of in-hospital stay was significantly shorter in the TR arm vs. the TF arm (7.2 days vs. 9.45 days, $p<0.05$). The corresponding indirect costs per patient were 138 EUR lower in the TR arm than in the TF arm (442 EUR vs. 580 EUR; Table 3). If all of the PCI in STEMI patients (28,060 procedures per year) were performed from a radial approach, the yearly savings from indirect costs would reach 2.58 x 10$^6$ EUR.

## 4. Discussion

The number of pharmacoeconomic publications assessing PCI in the STEMI population is limited, and we have not found a single cost analysis based on a randomized control trial comparing TR vs. TF in a STEMI population.

One of the first studies that assessed the costs of non-acute PCI in relation to vascular access was published by Mann et al.[11] They showed that the TR approach was substantially less expensive than the TF approach because of lower supply costs and fewer access complications. The authors suggested that that the TR approach should become the dominant strategy for coronary stenting because the approach offered better outcomes at a lower cost.

A study of paramount importance conducted in 2007 addressed the problem of cost-effectiveness from the TR approach by comparing it with TF access performed with and without closure device.[12] The equipment cost was higher in the TR group compared to the TF group without a vascular closure device (93.0 ± 9.5 USD vs. 40.5 USD, $p<0.001$) but lower than costs in the TF group with a vascular closure device (19.7 ± 12.7 USD vs. 31.1 ± 9.3 USD, $p < 0.001$). The total variable procedural cost was lower for the TR group than the cost for both TF groups, which was mainly driven by lower recovery costs in the TR group associated with shorter stays in the recovery room (369.5 USD ± 74.6 vs. 446.9 USD ± 60.2 and 553.4 USD ± 81.0; $p < 0.001$). These findings were consistent with our results, although there are some crucial differences between the two studies. The previous study was not dedicated to STEMI, and it was conducted in the US health care system. Additionally, the authors did not assess the total length and cost of the hospital stays, and they did not analyze

**Table 2** In-hospital costs

| | Radial access (n=52) | | | Femoral access (n=51) | | | p |
|---|---|---|---|---|---|---|---|
| | Average ± SD [EUR] | Min [EUR] | Max [EUR] | Average ± SD [EUR] | Min [EUR] | Max [EUR] | |
| Total cost | 2,740 ± 744.5 | 1,177.8 | 4,847.6 | 2,686.8 ± 1,316.8 | 979.7 | 9,925.5 | 0.80 |
| Medical costs | 2,343.9 ± 579.8 | 94.3 | 990.6 | 2,296.5 ± 1027.2 | 47.2 | 2,311.3 | 0.77 |
| Hospital stay and pharmacotherapy | 1,469.3 ± 555.1 | 1,083.5 | 3,857.1 | 1,421.7 ± 889.9 | 932.5 | 7614.2 | 0.87 |
| Cath lab costs | 139.4 ± 59.6 | 613.2 | 3077.8 | 130 ± 68.7 | 306.6 | 6709.9 | 0.45 |
| Procedural single-use materials (stents, balloons, wires, etc.) | 566.7 ± 308.33 | 16.3 | 265.3 | 585.6 ± 363.6 | 17 | 371.5 | 0.78 |
| Periprocedural pharmacotherapy | 149.8 ± 149.6 | 24.8 | 1,726.7 | 142.9 ± 147 | 24.8 | 1,818.6 | 0.82 |
| Unplanned diagnostics | 17.9 ± 27.6 | 0 | 318.6 | 17.9 ± 22 | 0 | 320.8 | 0.99 |
| Non-medical costs | 396.5 ± 199.5 | 0 | 681.1 | 390.3 ± 319.4 | 0 | 138.9 | 0.91 |

SD — standard deviation; EUR — Euro; Conversion rate: 1 EUR = 4.24 Polish zloty.

**Table 3** Extrapolation of indirect cost onto the Polish population.

| | Radial access | Femoral access | Total |
|---|---|---|---|
| pPCI in STEMI patients *per year* | 9,353 | 18,707 | 28,060 |
| Length of hospitalization (days) | 7.20* | 9.45** | 8.20 |
| Average indirect cost related to sick leave | 437 EUR | 575 EUR | 529 EUR |
| Indirect costs (Poland) | 4,087,261 EUR | 10,756,525 EUR | 14,843,786 EUR |

pPCI — primary percutaneous coronary intervention; EUR — euro.
Conversion rate: 1 EUR = 4.24 Polish zloty.
*n=52; **n=51.

the indirect costs as well as the impact on the social cost burden.

The recently published analysis by Applegate et al. evaluated the costs related to TR vs. TF coronarography. The radial strategy was associated with a cost-benefit of 228 USD per procedure per patient (TR: 8,888 ± 7,994 USD vs. TF: 9,116 ± 8,299 USD). [13] The observed difference was mainly derived from shorter in-hospital stays, and the procedure-related costs were 17 USD higher in the TR group. A retrospective analysis of data from 20% of all unselected PCI gathered in the American PREMIER registry showed similar results.[14] The total in-hospital costs were 553 USD lower in the TR group [TR: 11,736 USD (95% CI: 11,200 — 12,272 USD) vs. 12,288 USD (95% CI: 12,102 — 12,474 USD), p=0.03]. Cooper et al. performed a randomized study assessing the cost and quality of life in patients who received coronary angiograms from TR vs. TF access.[15] The radial approach was associated with a marked decrease in hospitalization and in-hospital pharmacotherapy costs (TR: 2,010 USD vs. TF: 2,299 USD, p<0.0001). There was also a significantly shorter hospital stay in the TR arm (TR: 3.6 days vs. 10.4 days, p<0.0001). Of note, the procedure, material and periprocedural pharmacotherapy costs were equivalent between the groups. These observations are similar to those reported in our study.

In our study, the total costs were mainly driven by hospitalization, pharmacotherapy (52.7%) and procedure costs (21.2%). As reported by the Dutch researchers who analyzed the costs in a STEMI population, the hospitalization costs corresponded to 35% of total costs (2,030 ± 3,679 EUR) and procedural costs corresponded to 24% of total costs (1,187 ± 2,172 EUR). The authors did not distinguish the costs according to vascular access type; however, they clearly showed a strong correlation between the length of hospital stay and the total cost. Diagnostic procedures performed from radial access allow for same-day discharge, which is the most cost-effective approach.

We have not found any publications evaluating indirect costs in STEMI patients treated from a TR vs. TF access point. There are different approaches to estimate the indirect costs in healthcare. For the purpose of our study, we used the human-capital approach based on the length of hospitalization and gross domestic product per capita as a unit cost source for productivity lost. Due to the lack of reliable data regarding the period of sick leave after hospitalization, sick leave was not included in the analysis. This may be a limitation that led to an underestimation of the real indirect cost impact. The presented results are based on a subanalysis of the OCEAN RACE trial in which the sample size analysis was based on clinical, not pharmacoeconomic, assumptions.

There is no doubt that the TR approach provides clear safety and efficacy advantages over the TF strategy, which was confirmed by multiple randomized trials and elegantly summarized in a 3,347-patient meta-analysis that showed shorter hospital stays, lower risk of major/minor bleeding and lower short-term mortality associated with the TR approach.[16] These clinical benefits translate directly into

economic advantages for TR approach, which were confirmed by our study.[17]

## 5. Conclusions

The TR approach is associated with a lower cost of therapeutic success, shorter length of hospital stays and lower indirect costs. Introduction of TR access as the default approach in all STEMI centers may significantly reduce the overall financial burden. These results can be used to support a local decision on the best approach for PCI.

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