**Sex Differences in Use of Intracoronary Imaging in Patients undergoing Percutaneous Coronary Intervention**

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Intracoronary imaging (ICI) in the form of intravascular ultrasound (IVUS) and optical coherence tomography (OCT) has evolved as a useful adjuvant procedural tool to optimize PCI results and improve clinical outcomes(1). Current European Association of Percutaneous Coronary Intervention (EAPCI) guidelines emphasize the use of ICI in selected patients, such as those undergoing PCI for left main stem disease, complex long lesions, and chronic total occlusions(1). Although ICI can provide useful information about the underlying atherosclerotic disease in men and women, ICI use may be particularly informative in women who have a higher incidence of non-obstructive CAD and spontaneous coronary artery dissection than men(2). We sought to examine sex-related temporal trends, differences in clinical and procedural characteristics and in-hospital outcomes stratified according to the use of ICI.

The study cohort comprised all adults aged ≥18 years undergoing PCI between 1st January 2006 and 31st December 2019 derived from the British Cardiovascular Intervention Society (BCIS) registry, and divided into ICI and non-ICI groups, stratified by sex. Baseline characteristics and outcomes were reported for ICI and non-ICI groups in men and women, and compared using Chi-square test or the Wilcox rank-sum test as appropriate. The Cochrane-Armitage test was used to examine any statistically significant difference in the temporal use of ICI stratified by sex. The data were assumed to be missing at random and imputed with multiple imputations using chained equations (3). All subsequent analyses were undertaken on the imputed dataset using multivariable logistic regression models using maximum likelihood estimation to determine the difference in risk of adverse outcomes for the ICI group compared to the non-ICI group.

From a total of 994,478 patients, 62,292 (8.4%) out of 738,616 men received ICI, whereas only 20,183 (7.9%) out of 255,862 women received ICI (P<0.001) during the study period. Women in the ICI group were likely to be older (mean age 67.2 vs 64.6 years), more likely to be an ethnic minority (17.1% vs 13.7%) , and undergo PCI for non-ST-elevation acute myocardial infarction (44.0% vs 37.7%) compared to men in the ICI group. Analysis of the angiographic profile of women who received ICI showed complex coronary artery disease with a higher prevalence of LMS disease (22.6% vs 3.0%), multi-vessel PCI (34.5% vs 18.6%), and a higher number (≥3) of lesions treated (12.0% vs 6.8%) compared to the non-ICI group. Compared to men in the ICI group, women received a smaller stent size (mean stent diameter 3.7mm vs 3.8mm) and had smaller stented segment length (mean stent length 29.2mm vs 32.0mm).

By the end of the study period, the absolute rates of ICI use were approximately 5% lower in women than men (women 14.5% vs men19.6%, p<0.001), particularly during the later study years. Additionally, female sex was independent negative predictor (OR 0.93 95%CI 0.91-0.96) of receipt of ICI. Use of ICI was consistently lower for all EAPCI recommended indications of ICI use, such as acute coronary syndrome (11.6% vs 12.3%, p<0.01), long lesions (13.1% vs 16.3%, p<0.01), chronic total occlusions (16.2% vs 18.3%, p<0.01), LMS PCI (55.1% vs 57.5%, p<0.01), in-stent restenosis (28.0% vs 30.7%), stent thrombosis (30.9% vs 34.9%, p<0.01), calcified lesion (36.6% vs 40.1%, p<0.01) and renal disease (17.4% vs 19.5%, p<0.01) in women compared to men. After adjusting for differences in clinical and angiographic characteristics, use of ICI was associated with lower odds of in-hospital mortality (OR 0.48; 95% CI, 0.44-0.53), MACCE (OR 0.75; 95% CI, 0.71-0.80) in men, and women (in-hospital mortality (OR 0.56; 95% CI, 0.48-0.64)), MACCE (OR 0.83; 95% CI, 0.76-0.91) compared to the non-ICI groups, respectively.

To the best of our knowledge, for the first time in literature, our study shows that the use of ICI was associated with lower odds of adjusted in-hospital mortality and MACCE in women, with a similar magnitude of benefit as that observed in men. Previous studies have demonstrated fundamental sex-based differences in the coronary anatomy, vessel size, plaque morphology, which may not be well distinguished on conventional angiography alone (4). Thus, ICI use may allow better characterization of plaque morphology, optimize stenting and improve procedural outcomes in women.

Another important finding from our study is the lower uptake of ICI in women, especially during the later study years. It is plausible that intracoronary imaging in the overall cohort was lower, and the data were inseparable during the earlier years. However, with the increased growth of ICI, the absolute rates of ICI use was approximately 5% lower in women compared to men particularly during the later study years. Women have a higher incidence of MINOCA (myocardial infarction with non-obstructive coronary disease), spontaneous coronary artery dissection (SCAD) and plaque erosions (2,5). Therefore, ICI may play an important role in establishing the diagnosis and guiding further management. Our study was limited by the lack of detailed data about intracoronary imaging such as stent expansion, edge dissection, mean luminal area and minimum stented area. Therefore, based on the ICI, we could not define any anatomical differences between men and women.

This real-world analysis of almost every PCI procedure undertaken in England and Wales revealed emerging sex differences in intracoronary imaging use. Despite a substantial rise in intracoronary imaging use, adoption in women is slowing, and female sex was an independent negative predictor of ICI use. Consequently, women are less likely to undergo ICI guided revascularization according to current recommendations from the EAPCI.

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**Table 1: Baseline, procedural characteristics and crude outcomes of patients undergoing intracoronary imaging compared to no intracoronary imaging stratified by sex**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Variable | Men: no ICI | Men: ICI | p-value | Women: no ICI | Women: ICI | p-value |
| Number of patients | 676324 (91.6%) | 62292 (8.4%) |  | 235679 (92.1%) | 20183 (7.9%) |  |
| Age, mean ± SD | 64.1 (11.6) | 64.6 (11.8) | <0.001 | 68.8 (11.7) | 67.2 (12.4) | <0.001 |
| Ethnicity  |  |  |
| White | 442175 (84.4%) | 34789 (81.6%) | <0.001 | 157964 (86.3%) | 11333 (82.9%) | <0.001 |
| BAME | 82006 (15.6%) | 7850 (18.4%) |  | 25059 (13.7%) | 2330 (17.1%) |  |
| Left Ventricular Ejection Fraction  |  |  |
| Good (LVEF >=50%) | 576041 (85.2%) | 51205 (82.2%) | <0.001 | 204155 (86.6%) | 17000 (84.2%) | <0.001 |
| Fair (LVEF 30%-49%) | 78676 (11.6%) | 8526 (13.7%) |  | 25244 (10.7%) | 2523 (12.5%) |  |
| Poor (LVEF <= 29%) | 21607 (3.2%) | 2561 (4.1%) |  | 6280 (2.7%) | 660 (3.3%) |  |
| Indication  |  |  |
| Stable | 262106 (38.8%) | 30389 (48.8%) | <0.001 | 85154 (36.1%) | 8812 (43.7%) | <0.001 |
| NSTEMI | 238471 (35.3%) | 23454 (37.7%) |  | 90856 (38.6%) | 8888 (44.0%) |  |
| STEMI | 174863 (25.9%) | 8093 (13.0%) |  | 59389 (25.2%) | 2342 (11.6%) |  |
| Smoking status |  |  |
| Non-smoker | 208856 (34.4%) | 19846 (35.1%) | <0.001 | 101568 (48.3%) | 8944 (48.7%) | <0.001 |
| Current smoker | 149528 (24.7%) | 10797 (19.1%) |  | 46554 (22.1%) | 3324 (18.1%) |  |
| Ex-smoker | 248136 (40.9%) | 25954 (45.9%) |  | 62204 (29.6%) | 6082 (33.1%) |  |
| Co-morbidities |  |  |
| Prior PCI (%) | 162759 (24.8%) | 26905 (44.1%) | <0.001 | 45518 (19.9%) | 7328 (37.2%) | <0.001 |
| Prior MI (%) | 179496 (28.1%) | 23454 (39.4%) | <0.001 | 51354 (23.0%) | 6348 (33.1%) | <0.001 |
| Prior CABG (%) | 67477 (10.3%) | 6293 (10.3%) | 0.75 | 14738 (6.4%) | 1435 (7.3%) | <0.001 |
| Diabetes (%) | 134287 (20.5%) | 14483 (23.8%) | <0.001 | 51859 (22.7%) | 5048 (25.6%) | <0.001 |
| Hypertension (%) | 347058 (53.6%) | 35611 (59.9%) | <0.001 | 137416 (60.7%) | 12344 (63.8%) | <0.001 |
| Hypercholesterolaemia | 372871 (57.5%) | 35504 (59.8%) | <0.001 | 132897 (58.7%) | 11583 (59.9%) | 0.001 |
| Renal disease (%) | 15851 (2.5%) | 2051 (3.4%) | <0.001 | 5233 (2.3%) | 574 (2.9%) | <0.001 |
| GPIIb/IIIa inhibitor use | 129254 (20.7%) | 9612 (16.9%) | <0.001 | 38391 (17.7%) | 2636 (14.3%) | <0.001 |
| Procedural characteristics  |  |  |
| Pressure Wire | 67592 (10.0%) | 7681 (12.3%) | <0.001 | 23333 (9.9%) | 2161 (10.7%) | <0.001 |
| In-stent restenosis | 23079 (4.4%) | 6156 (15.2%) | <0.001 | 7036 (3.9%) | 1962 (14.7%) | <0.001 |
| Number of lesions treated  |  |  |
| 1 | 397047 (69.7%) | 25904 (58.8%) | <0.001 | 141950 (72.0%) | 9038 (62.3%) | <0.001 |
| 2 | 128736 (22.6%) | 12167 (27.6%) |  | 41836 (21.2%) | 3733 (25.7%) |  |
| ≥3 | 44089 (7.7%) | 6003 (13.6%) |  | 13440 (6.8%) | 1745 (12.0%) |  |
| Number of stents used  |  |  |
| 0 | 47943 (8.5%) | 5249 (11.9%) | <0.001 | 17205 (8.8%) | 1752 (12.1%) | <0.001 |
| 1 | 299980 (53.0%) | 17124 (38.9%) |  | 107113 (54.7%) | 6103 (42.1%) |  |
| 2 | 142130 (25.1%) | 11593 (26.4%) |  | 47616 (24.3%) | 3760 (26.0%) |  |
| ≥3 | 75647 (13.4%) | 10028 (22.8%) |  | 23753 (12.1%) | 2867 (19.8%) |  |
| Number of vessels treated |  |  |
| 1 | 526611 (80.3%) | 40018 (66.7%) | <0.001 | 186734 (82.1%) | 13269 (68.8%) | <0.001 |
| 2 | 109093 (16.6%) | 14371 (24.0%) |  | 34535 (15.2%) | 4323 (22.4%) |  |
| ≥3 | 19941 (3.0%) | 5576 (9.3%) |  | 6148 (2.7%) | 1695 (8.8%) |  |
| Directional/rotational atherectomy | 11388 (1.9%) | 3184 (6.2%) | <0.001 | 4344 (2.1%) | 1026 (6.2%) | <0.001 |
| Access site  |  |  |
| Femoral | 218047 (33.2%) | 12204 (20.0%) | <0.001 | 84874 (37.1%) | 5433 (27.5%) | <0.001 |
| Radial | 417092 (63.4%) | 44290 (72.5%) |  | 135200 (59.0%) | 12915 (65.4%) |  |
| Multiple Access | 22521 (3.4%) | 4612 (7.5%) |  | 8987 (3.9%) | 1387 (7.0%) |  |
| LMS PCI | 20557 (3.1%) | 12298 (20.5%) | <0.001 | 6855 (3.0%) | 4365 (22.6%) | <0.001 |
| Multi-vessel PCI | 132489 (20.2%) | 22114 (36.9%) | <0.001 | 42243 (18.6%) | 6675 (34.5%) | <0.001 |
| Chronic Total Occlusion PCI | 42682 (8.1%) | 3532 (8.4%) | 0.011 | 11004 (6.0%) | 788 (5.7%) | 0.13 |
| Stent Length | 25.8 (14.0) | 32.0 (19.7) | <0.001 | 24.8 (13.5) | 29.2 (18.2) | <0.001 |
| Stent Diameter | 3.3 (0.6) | 3.8 (0.7) | <0.001 | 3.2 (0.5) | 3.7 (0.7) | <0.001 |
|  Crude Outcomes  |  |  |
| In-hospital MACCE | 17731 (2.6%) | 1518 (2.4%) | 0.006 | 8099 (3.4%) | 632 (3.1%) | 0.022 |
| In-hospital mortality | 9347 (1.4%) | 561 (0.9%) | <0.001 | 4922 (2.1%) | 275 (1.4%) | <0.001 |
| Bleeding complications  | 2314 (0.3%) | 264 (0.4%) | <0.001 | 1954 (0.8%) | 213 (1.1%) | <0.001 |
| Adjusted outcomes | **Reference** | **Odds Ratio** | **95% CI** | **Reference** | **Odds ratio** | **95%CI** |
| In-hospital MACCE | - | 0.75  | 0.71-0.80 | - | 0.83 | 0.76-0.91 |
| In-hospital mortality | - | 0.48 | 0.44-0.53 | - | 0.56 | 0.48-0.64 |
| Bleeding complications | - | 1.19 | 1.03-1.37 | - | 1.28 | 1.09-1.50 |

Abbreviations: BMI, body mass index; CCS, Canadian Cardiovascular Society; ECG, electrocardiogram; NYHA, New York Heart Association; PCI, percutaneous intervention; MI, myocardial infarction; GP, glycoprotein; IVUS, intravascular ultrasound; LMS, left main stem; LAD, left anterior descending; LCX, left circumflex artery; MACCE, major adverse cardiac and cerebrovascular events, ICI: Intracoronary imaging

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