Comparison of Characteristics and Complications in Men versus Women Undergoing Chronic Total Occlusion Percutaneous Intervention

Vinoda Sharma MBBS[a], William Wilson MBBS[b], William Smith MD[c], Margaret McEntegart MD PhD[d], Keith Oldroyd MD[d], Novalia Sidik MD[d], Alan Bagnall PhD[e], Mohaned Egred MD[e], John Irving MD[f], Julian Strange MD[g], Thomas Johnson MBBS MD[g], Simon Walsh, MD[h] Colm Hanratty MD[h], James Spratt MD[i *]

[a] Peter Munk Cardiac Centre, Toronto General Hospital, Toronto, Canada; [b] Royal Melbourne Hospital, Melbourne, Australia; [c]Trent Cardiac Centre, Nottingham City Hospital, Nottingham, UK; [d] Golden Jubilee National Hospital, Glasgow, UK; [e] Freeman Hospital, Newcastle-upon-Tyne, UK; [f] Ninewells Hospital, Dundee, UK; [g] University Hospitals Bristol, Bristol, UK; [h] Belfast City Hospital, Belfast, UK; [i] Forth Valley Royal Hospital, Larbert, UK

*** Corresponding Author:**

Dr James Spratt BSc, MD, FRCP, FESC, FACC

Consultant Cardiologist

Address for Correspondence:

Forth Valley Royal Hospital

Stirling Road

Larbert

FK5 4WR

Phone: +44 7816 615315

Fax: +44 7816 615315

Email: James.spratt@nhs.net

Running head: Gender and CTO PCI

Funding Sources: None

Abstract:

Gender differences exist in clinical outcomes following routine PCI, but studies reporting such outcomes following CTO PCI are limited. We assessed the characteristics and outcomes of female patients undergoing chronic total occlusion (CTO) percutaneous coronary intervention (PCI).We retrospectively analysed a dedicated national (United Kingdom) prospective CTO database from 2011-2015 for outcomes and characteristics of female patients undergoing CTO PCI (unmatched and propensity matched). Female patients constituted 20.5% (n=260/1271) of the un-matched cohort and 33.3% (n=233/699) of the matched cohort and were more likely to be older (> 70 years of age females, 48% in the unmatched and 45% in the matched cohort). An increased in-hospital complication rate was observed in female patients (unmatched: 10% females versus 4.45% males, p=0.0012 and matched 9.87% females versus 3.86% males, p=0.0032). Coronary perforation, bleeding and contrast induced nephropathy (CIN) were more frequently observed in female patients. Femoral access site with > 6 French sheath was associated with an increased risk of bleeding. Presence of calcification in the CTO artery was associated with coronary perforation (grade III) in female patients in the matched cohort (p=0.007). Female patients undergoing CTO PCI were older and experienced increased of in-hospital complications. Increased awareness of these complications could influence the selection of access site and sheath size, the need for pre-hydration, judicious choice of balloon size, collateral selection and wire placement in female patients undergoing CTO PCI.

Keywords: chronic total occlusion, gender differences, percutaneous coronary intervention

Introduction:

Chronic Total Occlusion (CTO) Percutaneous Intervention (PCI) has generated increasing interest with the availability of new techniques and tools resulting in improved success rates, despite an increase in the complexity of arteries treated [1]. However, data regarding gender differences in CTO PCI are limited. Female patients are under-represented in published CTO PCI literature with the proportion of female patients varying from 14% to 21% [2-5]. Although similar procedural success rates are seen in both men and women undergoing CTO PCI, a greater reduction in mortality has been reported in the male cohort [3], potentially suggesting an unequal benefit of CTO PCI in male patients. It is well documented that gender differences exist in clinical outcomes following routine PCI [6-8], but studies reporting such outcomes following CTO PCI are very limited. We aimed therefore to assess the characteristics and complications (in-hospital and 30-day outcomes) of female patients, when compared to their male counterparts undergoing CTO PCI.

Methods:

Dedicated, expert CTO PCI operators (lifetime experience of >300 cases per operator) from the United Kingdom prospectively enter baseline, procedural and outcome details into an anonymised online audit tool for consecutive CTO PCI cases. Participation is entirely voluntary and non/pre proctored CTO operators do not contribute to this database. We retrospectively analysed this database for outcomes and characteristics of patients undergoing CTO PCI from June 2011 to February 2015. Patients who had more than one CTO treated by PCI were entered as separate procedures. For patients who required more than one PCI attempt for the same CTO, only the final procedure was included. Demographics, procedural variables, procedural complications and success rates (including success for the first CTO PCI attempt) were compared between male and female patients. CTOs were defined as lesions with angiographic evidence of a total occlusion with thrombolysis in myocardial infarction (TIMI) 0 grade flow and estimated occlusion duration of >3 months[1]. Procedural success was defined as restoration of antegrade TIMI 3 flow with <30% residual stenosis within the treated segment[1]. Definitions of other procedural characteristics are as described in detail by Wilson et al[1].

In-hospital complications evaluated included were a composite of coronary perforation (Ellis grade III), acute vessel closure, bleeding (according to site- local haematoma, retroperitoneal or gastrointestinal), peri-procedural myocardial infarction (MI: chest pain +/- ECG changes with typical rise and fall of cardiac biomarkers), transient ischaemic attack (TIA)/stroke, contrast induced nephropathy (CIN: acute kidney injury leading to dialysis or leading to an increase in serum Creatinine >25% from baseline) and death. Follow-up complications included composite of stent thrombosis, TIA/stroke, MI at 30 days and death.

SPSS version 20 was used for statistical analysis (IBM Corporation, Armonk, NY, USA). Missing variables were replaced by mean of nearest neighbour. Variables with >10% missing data were excluded. Categorical variables were presented as percentage and continuous variables as mean (± standard deviation). Differences in categorical variables were tested by the chi-square or Fisher's exact test and differences in continuous variables by the student's t test or Mann Whitney U test. Variables were tested for normality and non–normal continuous variables were log transformed for inclusion in the analysis. To overcome the limitations of the observational nature of our study, we performed a propensity score matched analysis and compared variables between males and females in both the unmatched and matched patient cohort. The propensity score was derived by regression analysis with gender as the dependent variable and the following variables included: age, chronic kidney disease (CKD), history of smoking, hypertension (HTN), diabetes mellitus (DM), history of stroke, previous history of coronary artery bypass graft (CABG) surgery, history of previous PCI, hypercholesterolemia, peripheral vascular disease (PVD) and family history of coronary artery disease (CAD).

Propensity score matching was performed (2:1 nearest neighbour) without replacement and with calipers (set at 0.2 of the standard deviation of the logit of the propensity score) [9]. We ensured balance in the propensity score of the matched samples by assessing the standardised difference in the mean propensity score (0.36) , the ratio of the variance of the score (1.22) in the two groups [10] and in addition single factor ANOVA demonstrated a Levene statistic $p>0.05$ indicative of no difference in the two groups. Demographics, procedural variables, procedural complications and success rates (including success for the first CTO PCI attempt) were compared again between male and female patients in this matched cohort.

Results:

Female patients constituted 20.5% (n=260) of the un-matched cohort of a total of 1271 and were significantly older, with almost half of the female population older than 70 years of age (table 1). Female patients were less likely to be smokers (current or ex) or have undergone CABG in the past (table 1) in the unmatched cohort. Lesion complexity, as defined by the JCTO score, was similar between the two groups (table 2). Final CTO PCI approach was similar between the groups, except for Retrograde Dissection Re-entry (RDR), which was more common in male patients (p=0.04, table 2). Fluoroscopy dose, procedural time, screening time and contrast load were all significantly lower in female patients. Success rates were no different, even taking into consideration first attempt at CTO PCI (table 2).

In-hospital complications were more common in females (females 10.0% versus males 4.45%, p=0.0012). Coronary perforation (Ellis III), bleeding complications and CIN were more frequent in female patients (table 3).

Both male and female patients in the unmatched cohort with coronary perforation were more likely to have calcification and tortuosity of the CTO artery ($p<0.01$ for all).

Propensity score matching was performed (2:1 nearest neighbour) without replacement and with calipers resulted in a cohort of 466 male patients matched to 233 females (2:1 matching) from the original database [9]. The matched group was assessed for differences in baseline, procedural characteristics and outcomes (table 4).

The 233 propensity score matched females demonstrated similar baseline characteristics as the unmatched female cohort (table 4). Female patients were older and less likely to be smokers or undergone previous CABG (table 4). Those >70 years constituted nearly half of the matched female population (45.1%, 105/233). Lesion complexity continued to be similar between female and male patients in the matched group (table 5).

Final CTO PCI approach was less likely to be RDR in women compared to men undergoing CTO PCI. Fluoroscopy dose and total contrast use were again significantly less in female patients. Success rates were similar (males 82.6% versus females 85%, p=ns) and continued to be >80% as in the unmatched cohort (table 5). Significantly increased in-hospital complications (females 9.87% versus males 3.86%, p=0.0032) i.e. coronary perforation (Ellis III), bleeding complications and CIN were more frequent in female patients (table 6). A significant association was only seen in female patients between coronary perforation and presence of calcification in the CTO artery (p=0.007).

Female patients in both the unmatched and matched cohorts with femoral access site sheath size > 6 French were more likely to have peripheral bleeds. Retroperitoneal bleeds were significantly more common in female patients in both the unmatched (1.9% females versus 0.5% males, p=0.035, table 3) and the matched cohort (2.1% females versus 0.4% males, p=0.04, table 6).

Neither in-hospital nor 30-day mortality occurred in the female cohort. Follow up outcomes at 30 days occurred in <2% of female patients (tables 3 and 6).

Discussion:

In this observational, propensity matched analysis of a prospective CTO PCI database, we have identified that women compared to men, present at an older age for CTO PCI and are less likely to have undergone previous CABG. Procedural time, fluoroscopy dose, screening time and contrast load were all significantly lower in female patients. Success rates were no different, even taking into consideration first attempt at CTO PCI (table 2). In-hospital complications were more common in females versus males in both the unmatched (females 10.0% versus males 4.45%, p=0.0012) and matched cohort (females 9.87% versus males 3.86%, p=0.0032). Specifically, coronary perforation (Ellis III), bleeding complications and CIN were more frequent in female patients (table 3).

The average age of women at presentation was greater compared to men (68.5 ± 9.8 vs. 64.2±10.3 p<0.0001). It may reflect the fact that women are in part protected from ischaemic heart disease pre-menopause so the disease process may simply be delayed. It is well recognised that women compared to men, may present later in the disease process or have treatment deferred due to gender bias[11,12]. Despite females making up 30-40% of angiographic coronary artery disease studies only 20% of our database population are female. In a large registry of patients undergoing diagnostic coronary angiography a CTO was identified in 18.4% of all cases (post CABG patients were excluded)[4] - females again made up only 20% of this group.

We know that despite a similar disease burden, women are more likely to be treated medically and less likely to be referred for CABG than male counterparts [4,13]. Placing a graft on an artery with a flow limiting stenosis will result in the lesion progressing to complete obstruction in up to 50% of cases in a 1 year period [14]. The Canadian registry identified a CTO in 54% of patients post CABG (compared with 18.4% without prior CABG) [4]. The fact that females are less likely to be referred for CABG may impact favourably on CTO formation. Our data supports this with 13.8 % of women having previous CABG versus 24.1% of males (table 1). There may well also be a referral bias against females with symptomatic CTO's.

While there are similar J-CTO scores between the groups there is a suggestion that the female cases were in fact less complex (tables 2 and 5). In the female patients there were lower fluoroscopy doses, procedure times, screening times and contrast doses with similar success rates compared to male patients. These indirectly suggest reduced complexity in this group.

Despite possible less complex anatomy the procedural complication rates were much higher in the female group. In hospital event rates occurred in 9.87% of females versus 3.86 % of matched males (Table 6). Over half of all events were bleeding related and in particular when the femoral sheath size was >6French (6.3% vs 2.1%, p=0.015). A previous CathPCI registry analysis has demonstrated that female patients have double the risk of bleeding complications [15]. The use of larger size femoral access sheaths was associated with an increased risk of bleeding. Female patients are known to have smaller diameter femoral arteries compared to males [16] and female gender is a known predictor of retroperitoneal bleeds [17]. Utilising the radial artery for at least one of the access sites or performing femoral access under ultrasound guidance [18]may help in reducing this complication. While all the operators use fluoroscopy to locate the femoral head and guide the femoral puncture using additional imaging modalities including ultrasound guidance to maximise the chance of a clean femoral puncture may have merit in this group[19].

The rates of grade 3 coronary perforations were higher in the unmatched (3.08% versus 0.5%, p=0.001) and matched female group compared to male patients (3.0 % versus 1.07%, p=ns) (tables 3 and 6). In routine PCI, known risk factors predisposing to coronary perforation include female gender, older age, treated hypertension and calcified arteries [20-25]. It appears that this increased risk of coronary perforation also occurs in females during CTO PCI. Intra-vascular Ultrasound (IVUS) studies have demonstrated that female coronary arteries are smaller even after adjusting for body surface area[26]. This may in part explain the higher perforation rates. We also established a correlation between the presence of calcification in the CTO artery and perforation. The final strategy was less commonly RDR in the female compared to the male group (both unmatched and matched cohorts, tables 2 and 5). We hypothesis that collateral channels in females may be more challenging to cross than in males due to smaller size, tortuosity and angulation, resulting in fewer RDR procedures.

Published registry data has demonstrated the incidence of CIN peri-PCI to be as high as 3.3% [27]. Despite use of reduced contrast load in female patients, the incidence of CIN in females was significantly greater than in their male counterparts in both the unmatched (females 1.2% versus males 0.2%, p=0.005) and matched cohorts (females 2.1% versus males 0.2%, p=0.017) (tables 3 and 6). CIN was significantly more frequent in female patients who underwent >1 CTO PCI procedure compared to male patients. None of the male patients who underwent > 1 CTO PCI procedure developed CIN. Older age, pre-existing renal failure and diabetes mellitus are known to be contributory to CIN [28], but female gender has not been shown to be a predictor of CIN post PCI. Most of the female patients (4 out of 5) who developed CIN were older than 70 years of age. A combination of older age and repeat procedures in female patients could have contributed to the higher incidence of CIN. As increased age >75 years is a risk factor for CIN [29], this may be a subset of patients who would benefit from more aggressive management of medications and hydration peri-procedure, especially if the first CTO PCI is a failure and further attempts are planned.

This study has a number of potential limitations. Participation in this registry is entirely voluntary but the contributing operators are all dedicated/proctored operators. While this might contribute to some bias, it is difficult to quantify because proctored operators are known to attempt CTOs with a higher J-CTO score (≥2) and demonstrate higher success rates with similar complication rates compared to non/pre-proctored operators [30]. Despite propensity matching, ours is an observational study. We have relied on the individual PCI centres to enter clinical data including complications into the database and there is the potential for under reporting. Some of the definitions of complications are operator dependent (e.g. bleeding) and validation of the complications is dependent on the clinical data input. In addition, data regarding details of dual antiplatelet therapy, dose of Heparin

or concurrent anticoagulation was not available. This could potentially create bias and influence bleeding outcomes. The number of female patients included in our study although similar to other CTO PCI studies (14-21 %), [2-5], still under-represents the female population. However, this is one of the first studies to evaluate characteristics and complications of female patients undergoing CTO PCI.

Acknowledgements

We acknowledge the contribution of Dr Vladimir Dzavik and Dr Christopher B Overgaard for their assistance in completing this manuscript

1. Wilson WW, Simon YA, Hanratty C; Bagnall A, Egred M, Smith E, Oldroyd K, McEntegart M, Irving J, Strange J, Douglas H, Spratt JC. Hybrid Approach Improves success of chronic total occlusion. *Heart* 2016 Sep;102(18):1486-1493

2. George S, Cockburn J, Clayton TC, Ludman P, Cotton J, Spratt J, Redwood S, de Belder M, de Belder A, Hill J, Hoye A, Palmer N, Rathore S, Gershlick A, Di Mario C, Hildick-Smith D, British Cardiovascular Intervention S, National Institute for Cardiovascular Outcomes R. Long-term follow-up of elective chronic total coronary occlusion angioplasty: analysis from the U.K. Central Cardiac Audit Database. *J Am Coll Cardiol* 2014;64:235-243.

3. Claessen BE, Chieffo A, Dangas GD, Godino C, Lee SW, Obunai K, Carlino M, Chantziara V, Apostolidou I, Henriques JP, Leon MB, Di Mario C, Park SJ, Stone GW, Moses JW, Colombo A, Mehran R, Multinational CTOR. Gender differences in long-term clinical outcomes after percutaneous coronary intervention of chronic total occlusions. *J Invasive Cardiol* 2012;24:484-488.

4. Fefer P, Knudtson ML, Cheema AN, Galbraith PD, Osherov AB, Yalonetsky S, Gannot S, Samuel M, Weisbrod M, Bierstone D, Sparkes JD, Wright GA, Strauss BH. Current perspectives on coronary chronic total occlusions: the Canadian Multicenter Chronic Total Occlusions Registry. *J Am Coll Cardiol* 2012;59:991-997.

5. Fefer P, Gannot S, Kochkina K, Maor E, Matetzky S, Raanani E, Guetta V, Segev A. Impact of coronary chronic total occlusions on long-term mortality in patients undergoing coronary artery bypass grafting. *Interact Cardiovasc Thorac Surg* 2014;18:713-716.

6. Peterson ED, Lansky AJ, Kramer J, Anstrom K, Lanzilotta MJ, National Cardiovascular Network Clinical I. Effect of gender on the outcomes of contemporary percutaneous coronary intervention. *Am J Cardiol* 2001;88:359-364.

7. Anderson ML, Peterson ED, Brennan JM, Rao SV, Dai D, Anstrom KJ, Piana R, Popescu A, Sedrakyan A, Messenger JC, Douglas PS. Short- and long-term outcomes of coronary stenting in women versus men: results from the National Cardiovascular Data Registry Centers for Medicare & Medicaid services cohort. *Circulation* 2012;126:2190-2199.

8. Lichtman JH, Wang Y, Jones SB, Leifheit-Limson EC, Shaw LJ, Vaccarino V, Rumsfeld JS, Krumholz HM, Curtis JP. Age and sex differences in inhospital complication rates and mortality after percutaneous coronary intervention procedures: evidence from the NCDR((R)). *Am Heart J* 2014;167:376-383.

9. Austin PC. Optimal caliper widths for propensity-score matching when estimating differences in means and differences in proportions in observational studies. *Pharm Stat* 2011;10:150-161.

10. Rubin DB. Using propensity scores to help design observational studies: application to the tobacco litigation. . *Health Services & Outcomes Research Methodology* 2001;2:169-188.

11. Ayanian JZ, Epstein AM. Differences in the use of procedures between women and men hospitalized for coronary heart disease. *N Engl J Med* 1991;325:221-225.

12. Daly C, Clemens F, Lopez Sendon JL, Tavazzi L, Boersma E, Danchin N, Delahaye F, Gitt A, Julian D, Mulcahy D, Ruzyllo W, Thygesen K, Verheugt F, Fox KM, Euro Heart Survey I. Gender differences in the management and clinical outcome of stable angina. *Circulation* 2006;113:490-498.

13. King SB, 3rd, Lembo NJ, Weintraub WS, Kosinski AS, Barnhart HX, Kutner MH, Alazraki NP, Guyton RA, Zhao XQ. A randomized trial comparing coronary angioplasty with coronary bypass surgery. Emory Angioplasty versus Surgery Trial (EAST). *N Engl J Med* 1994;331:1044-1050.

14. Maurer BJ, Oberman A, Holt JH, Jr., Kouchoukos NT, Jones WB, Russell RO, Jr., Reeves TJ. Changes in grafted and nongrafted coronary arteries following saphenous vein bypass grafting. *Circulation* 1974;50:293-300.

15. Daugherty SL, Kim S, Thompson L, Rao S, Subherwal S, Tsai T, Messenger J, Masoudi F. GENDER AND BLEEDING RISK FOLLOWING PERCUTANEOUS CORONARY INTERVENTIONS: A CONTEMPORARY REPORT FROM THE NCDR®. *J Am Coll Cardiol* 2012;59:E1803-E1803.

16. Schnyder G, Sawhney N, Whisenant B, Tsimikas S, Turi ZG. Common femoral artery anatomy is influenced by demographics and comorbidity: implications for cardiac and peripheral invasive studies. *Catheter Cardiovasc Interv* 2001;53:289-295.

17. Farouque HM, Tremmel JA, Raissi Shabari F, Aggarwal M, Fearon WF, Ng MK, Rezaee M, Yeung AC, Lee DP. Risk factors for the development of retroperitoneal hematoma after percutaneous coronary intervention in the era of glycoprotein IIb/IIIa inhibitors and vascular closure devices. *J Am Coll Cardiol* 2005;45:363-368.

18. Seto AH, Abu-Fadel MS, Sparling JM, Zacharias SJ, Daly TS, Harrison AT, Suh WM, Vera JA, Aston CE, Winters RJ, Patel PM, Hennebry TA, Kern MJ. Real-time ultrasound guidance facilitates femoral arterial access and reduces vascular complications: FAUST (Femoral Arterial Access With Ultrasound Trial). *JACC Cardiovasc Interv* 2010;3:751-758.

19. Fairley SL, Lucking AJ, McEntegart M, Shaukat A, Smith D, Chase A, Hanratty CG, Spratt JC, Walsh SJ. Routine Use of Fluoroscopic-Guided Femoral Arterial Puncture to Minimise Vascular Complication Rates in CTO Intervention: Multi-centre UK experience. *Heart Lung Circ* 2016.

20. Fasseas P, Orford JL, Panetta CJ, Bell MR, Denktas AE, Lennon RJ, Holmes DR, Berger PB. Incidence, correlates, management, and clinical outcome of coronary perforation: analysis of 16,298 procedures. *Am Heart J* 2004;147:140-145.

21. Ellis SG, Ajluni S, Arnold AZ, Popma JJ, Bittl JA, Eigler NL, Cowley MJ, Raymond RE, Safian RD, Whitlow PL. Increased coronary perforation in the new device era. Incidence, classification, management, and outcome. *Circulation* 1994;90:2725-2730.

22. Hennessy TG, McCann HA, Sugrue DD. Fatal stent thrombosis following successful treatment or coronary artery rupture in an octogenarian. *Cathet Cardiovasc Diagn* 1997;42:434-436.

23. Reimers B, von Birgelen C, van der Giessen WJ, Serruys PW. A word of caution on optimizing stent deployment in calcified lesions: acute coronary rupture with cardiac tamponade. *Am Heart J* 1996;131:192-194.

24. Shimony A, Zahger D, Van Straten M, Shalev A, Gilutz H, Ilia R, Cafri C. Incidence, risk factors, management and outcomes of coronary artery perforation during percutaneous coronary intervention. *Am J Cardiol* 2009;104:1674-1677.

25. Al-Lamee R, Ielasi A, Latib A, Godino C, Ferraro M, Mussardo M, Arioli F, Carlino M, Montorfano M, Chieffo A, Colombo A. Incidence, predictors, management, immediate and long-term outcomes following grade III coronary perforation. *JACC Cardiovasc Interv* 2011;4:87-95.

26. Dodge JT, Jr., Brown BG, Bolson EL, Dodge HT. Lumen diameter of normal human coronary arteries. Influence of age, sex, anatomic variation, and left ventricular hypertrophy or dilation. *Circulation* 1992;86:232-246.

27. Rihal CS, Textor SC, Grill DE, Berger PB, Ting HH, Best PJ, Singh M, Bell MR, Barsness GW, Mathew V, Garratt KN, Holmes DR, Jr. Incidence and prognostic importance of acute renal failure after percutaneous coronary intervention. *Circulation* 2002;105:2259-2264.

28. Mehran R, Nikolsky E. Contrast-induced nephropathy: definition, epidemiology, and patients at risk. *Kidney Int Suppl* 2006:S11-S15.

29. MEENA (A Randomized Controlled Trial for the Prevention of Contrast-induced Nephropathy with Sodium Bicarbonate in Persons Undergoing Coronary Angiography). *Clin Cardiol* 2007;30:416-416.

30. Sharma V, Jadhav ST, Harcombe AA, Kelly PA, Mozid A, Bagnall A, Richardson J, Egred M, McEntegart M, Shaukat A, Oldroyd K, Vishwanathan G, Rana O, Talwar S, McPherson M, Strange JW, Hanratty CG, Walsh SJ, Spratt JC, Smith WH. Impact of proctoring on success rates for percutaneous revascularisation of coronary chronic total occlusions. *Open Heart* 2015;2:e000228.

Table 1

Table 1: Baseline characteristics of unmatched patients

Variable	Men	Women	Significance
	n=1011	n=260	p value
Age in years	64.2±10.3	68.5±9.8	p<0.0001
>70 years	289 (28.6%)	125 (48.1%)	p<0.0001
Hypertension	684 (67.7%)	190 (73.1%)	p=0.10
Hypercholesterolemia	690 (68.2%)	184 (70.8%)	p=0.45
Diabetes Mellitus	250 (24.7%)	62 (23.8%)	p=0.81
Smoker	696 (68.8%)	136 (52.3%)	p=<0.0001
Angina (CCS class >2)	476 (47.1%)	142 (54.6%)	p=0.03
Previous TIA*/Stroke	50 (4.9%)	11 (4.2%)	p=0.75
Previous Myocardial Infarction	559 (55.3%)	134 (51.4%)	p=0.30
Previous coronary bypass	244 (24.1%)	36 (13.8%)	p<0.001
Chronic Kidney Disease	129 (12.8%)	38 (14.6%)	p=0.41
Family History of CAD†	337 (33.3%)	90 (34.6%)	p=0.71
Previous PCI‡	566 (56.0%)	135 (51.9%)	p=0.26
Peripheral Vascular Disease	107 (10.6%)	28 (10.8%)	p=0.91

TIA*: Transient Ischaemic Attack; CAD†: Coronary Artery Disease; PCI‡: Percutaneous Coronary Intervention

Table 2: Procedural characteristics of unmatched patients

Variable	Men n=1011	Women n=260	Significance p value
CTO* coronary artery RCA†	516 (51.0%)	155 (59.6%)	p=0.01
Access site femoral	859 (85.0%)	226 (86.9%)	p=0.49
Femoral access site >6French	779 (77.1%)	202 (77.7%)	p=0.87
J-CTO‡ score ≥2	748 (74.0%)	188 (72.3%)	p=0.58
J-CTO‡ score 0	91 (9.0%)	20 (7.7%)	-
J-CTO‡ score 1	172 (17.0%)	52 (20%)	-
J-CTO‡ score 2	240 (23.7%)	67 (25.8%)	-
J-CTO‡ score 3	227 (22.5%)	64 (24.6%)	-
J-CTO‡ score 4	222 (22.0%)	44 (16.9%)	-
J-CTO‡ score 5	59 (5.8%)	13 (5.0%)	-
Single CTO PCI§ procedure	840 (83.1%)	232 (89.2%)	p=0.016
Primary CTO PCI§ approach			
Antegrade Wire Escalation	670 (66.3%)	184 (70.8%)	p=0.18
Antegrade Dissection Re-entry	95 (9.4%)	29 (11.2%)	p=0.41
Retrograde Wiring	119 (11.8%)	23 (8.8%)	p=0.22
Retrograde Dissection Re-entry	127 (12.6%)	24 (9.2%)	p=0.16
Final CTO PCI§ approach			
Antegrade Wire Escalation	444 (43.9%)	127 (48.8%)	p=0.16
Antegrade Dissection Re-entry	243 (24.0%)	59 (22.7%)	p=0.68
Retrograde Wiring	75 (7.5%)	26 (10%)	p=0.71
Retrograde Dissection Re-entry	249 (24.6%)	48 (18.5%)	p=0.04
Fluoroscopy dose (cGy/m2)¶	14712±9743.66	10170±8388.48	p<0.0001
Procedure time	111±48.7	104±43.9	p=0.05
Screening Time in minutes	43±23.8	38±19.8	p=0.02
Contrast load in milliliters (ml)	323±131.06	294±118.06	p=0.002
Success -single CTO PCI procedure	764/840 (91.0%)	209/232 (90.1%)	p=0.70
Success -all patients	833 (82.4%)	221 (85%)	p=0.36
Failure due to sub-intimal passage and inability to re-enter true lumen	89/178 (50%)	23/39 (59.0%)	p=0.38

CTO*: Chronic Total Occlusion; RCA†: Right Coronary Artery; J-CTO‡: Japanese CTO score; PCI§: Percutaneous Coronary Intervention; (cGy/m2)¶: CentiGrey per square meter

Table 3: Details of Complications in unmatched cohort

Variable	Men n=1011	Women n=260	Significance p value
In-hospital outcomes (composite)	45(4.45%)	26 (10.0%)	p=0.001
Coronary Perforation Ellis Grade III	5 (0.50%)	8 (3.08%)	p=0.001
Acute Vessel Closure	5 (0.50%)	2 (0.80%)	p=0.64
Bleeding	25 (2.50%)	15 (5.80%)	p=0.02
-Retroperitoneal bleed	5 (0.5%)	5 (1.9%)	p=0.04
-Femoral access>6French	23 (3.0%)	14 (6.9%)	p=0.01
Peri-procedural MI*	9 (0.9%)	3 (1.2%)	p=0.72
TIA†/Stroke	3 (0.3%)	1 (0.4%)	p=1.00
CIN‡ (all patients)	2 (0.2%)	5 (1.9%)	p=0.005
CIN‡ (patients >1 CTO PCI procedure)	0/171 (0%)	3/29 (10.3%)	p=0.003
Death	2 (0.2%)	0 (0%)	p=1.00
Follow-up outcomes (30 days composite)	14 (1.4%)	5 (1.9%)	p=0.57
Stent thrombosis	9 (0.9%)	1 (0.4%)	p=0.70
- Definite	7	0	-
- Probable	1	0	-
- Possible	1	1	-
TIA†/Stroke	0 (0%)	1 (0.4%)	p=0.20
MI*	5 (0.5%)	3 (1.2%)	p=0.21
Death	0 (0%)	0 (0%)	-

MI*: Myocardial Infarction; TIA†: Transient Ischemic Attack; CIN‡: Contrast Induced Nephropathy

Table 4: Baseline characteristics of matched patients

Variable	Men n=466	Women n=233	Significance p value
Age in years	66.0±10.1	68.±9.7	p=0.01
>70 years	164 (35.2%)	105 (45.1%)	p=0.01
Hypertension	320 (68.7%)	170 (73.0%)	p=0.26
Hypercholesterolemia	320 (68.7%)	164 (70.4%)	p=0.66
Diabetes Mellitus	132 (28.3%)	58 (24.9%)	p=0.37
Smoker	305 (65.5%)	129 (55.4%)	p=0.01
Angina (CCS class >2)	226 (48.5%)	128 (54.9%)	p=0.13
Previous TIA*/Stroke	31 (6.7%)	11 (4.7%)	p=0.40
Previous Myocardial Infarction	262 (56.2%)	122 (52.4%)	p= 0.33
Previous coronary bypass	93 (20.0%)	34 (14.6%)	p=0.10
Chronic Kidney Disease	61 (13.1%)	37 (15.9%)	p=0.36
Family History of CAD†	148 (31.8%)	84 (36.1%)	p=0.27
History of previous PCI‡	263 (56.4%)	122 (52.4%)	p=0.33
Peripheral Vascular Disease	59 (12.7%)	27 (11.6%)	p=0.72

TIA*: Transient Ischaemic Attack; CAD†: Coronary Artery Disease; PCI‡: Percutaneous Coronary Intervention

Table 5

Table 5: Procedural characteristics of matched patients

Variable	Male patients n=466	Female Patients n=233	Significance p value
CTO* coronary artery RCA†	245 (52.6%)	140 (60.1%)	p=0.06
Access site femoral	387 (83.0%)	202 (86.7%)	p=0.23
Femoral access site >6French	379 (81.3%)	191 (82.0%)	p=0.92
J-CTO‡ score ≥2	354 (76.0%)	169 (72.5%)	p=0.36
J-CTO‡ score 0	41 (8.8%)	18 (7.7%)	-
J-CTO‡ score 1	71 (15.2%)	46 (19.7%)	-
J-CTO‡ score 2	127 (27.3%)	61 (26.2%)	-
J-CTO‡ score 3	97 (20.8%)	55 (23.6%)	-
J-CTO‡ score 4	107 (23.0%)	40 (17.2%)	-
J-CTO‡ score 5	23 (4.9%)	13 (5.6%)	-
Single CTO PCI§ procedure	379 (81.33%)	205 (88.0%)	p=0.03
Primary CTO PCI§ approach			
Antegrade Wire Escalation	306 (65.7%)	163 (70.0%)	p=0.27
Antegrade Dissection Re-entry	45 (9.7%)	27 (11.6%)	p=0.43
Retrograde Wiring	58 (12.4%)	21 (9.0%)	p=0.21
Retrograde Dissection Re-entry	57 (12.2%)	22 (9.4%)	p=0.31
Final CTO PCI§ approach			
Antegrade Wire Escalation	214 (45.9%)	110 (47.2%)	p=0.75
Antegrade Dissection Re-entry	112 (24.0%)	55 (23.6%)	p=0.93
Retrograde Wiring	34 (7.3%)	23 (9.9%)	p=0.24
Retrograde Dissection Re-entry	106 (22.7%)	45 (19.3%)	p=0.33
Fluoroscopy dose (cGy/m2)¶	14205±9764.22	10434±8617.52	p<0.0001
Procedure time	109±47.2	105±44.5	p=0.50
Screening Time in minutes	41±22.6	39±20.2	p=0.22
Contrast load in milliliters (ml)	322±133.7	298±121.7	p=0.06
Success rate in single CTO PCI procedure	341/379 (89.9%)	182/205 (88.8%)	p=0.23
Success rate in all patients	385 (82.6%)	198 (85%)	p=0.45
Failure due to sub-intimal passage and inability to re-enter true lumen	44/81 (54.3%)	22/35 (62.9%)	p=0.42

CTO*: Chronic Total Occlusion; RCA†: Right Coronary Artery; J-CTO‡: Japanese CTO score; PCI§: Percutaneous Coronary Intervention; (cGy/m2)¶: CentiGrey per square meter

Table 6: Details of complications in matched cohort

Variable	Male patients n=466	Female Patients n=233	Significance p value
In-hospital outcomes (composite)	18 (3.86%)	23 (9.87%)	p=0.003
Coronary Perforation Ellis Grade III	5 (1.07%)	7 (3.0%)	p=0.12
Acute Vessel Closure	2 (0.4%)	2 (0.9%)	p=0.60
Bleeding	8 (1.7%)	13 (5.6%)	p=0.008
-Retroperitoneal bleed	2 (0.4%)	5 (2.1%)	p=0.04
-Femoral access>6French	8 (2.1%)	12 (6.3%)	p=0.015
Peri-procedural MI*	3 (0.6%)	3 (1.3%)	p=0.41
TIA†/Stroke	2 (0.4%)	1 (0.4%)	p=1.00
CIN‡ (all patients)	1 (0.2%)	5 (2.1%)	p=0.017
CIN‡ (patients >1 CTO PCI procedure)	0/86 (0%)	3/28 (10.7%)	p=0.014
Death	1 (0.2%)	0 (0%)	p=1.00
Follow-up outcomes (30 days composite)	7 (1.5%)	4 (1.7%)	p=1.00
Stent thrombosis	4 (0.9%)	0 (0%)	p=0.31
- Definite	2	0	-
- Probable	1	0	-
- Possible	1	0	-
TIA†/Stroke	0 (0%)	1 (0.4%)	p=0.33
MI*	3 (0.6%)	3 (1.3%)	p=0.41
Death	0 (0%)	0(0%)	p=1.00

MI*: Myocardial Infarction; TIA†: Transient Ischemic Attack; CIN‡: Contrast Induced Nephropathy

Author Disclosures

Click here to download Electronic Supplementary Material (online publication only): author_disclosures.docx