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Validation of the newly introduced CASTLE Score for predicting successful CTO recanalization

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ABSTRACT

Background: The new EuroCTO CASTLE Score was validated against the widely adopted Japanese Multicenter CTO Registry (J-CTO) score in predicting technical success in percutaneous coronary intervention (PCI) for coronary chronic total occlusions (CTO).

Methods: A total of 463 patients treated by CTO PCI were included in a retrospective analysis. Result: The mean CASTLE score was 2.23 ± 1.1 and J-CTO score was 2.84 ± 1.0. The overall technical success rate was 83.2%. At 30 days follow up, a primary composite safety endpoint showed a low proportion of stent thrombosis (0.2%) and re-hospitalization (0.4%). Moreover, an improvement of clinical symptoms was found in 83% of patients. Receiver operating characteristic analysis (ROC) demonstrated a comparable overall discriminatory performance in predicting technical outcome: CASTLE score, area under the ROC curve (AUC) 0.668, 95% CI: 0.606–0.730; J-CTO score AUC 0.692, 95% CI: 0.631–0.752; Comparison of AUCs: $p = 0.324$. Those findings were even consistent in more complex procedures CASTLE Score ≥ 4 and J-CTO score ≥ 3: CASTLE Score AUC 0.514, 95% CI: 0.409–0.619; J-CTO score, AUC 0.617, 95% CI: 0.493–0.741; Comparison of AUCs: $p = 0.211$. Furthermore, increasing score values are accompanied by a longer examination and fluoroscopy time, more contrast medium and a higher dose area product.

Conclusion: Compared to the widely accepted J-CTO score, the new introduced EuroCTO CASTLE score demonstrated a comparable overall discriminatory performance in predicting technical outcomes in CTO PCI.

1. Introduction

Recanalization of chronic total occlusion (CTO) still remains a challenging procedure in interventional cardiology. A CTO of a coronary artery can be identified in up to 18% among patients with a clinical indication for coronary angiography [1]. With the advent of novel recanalization techniques and emerging devices, percutaneous coronary intervention (PCI) has become a promising leading treatment option for these patients [2–7].

For a precise selection of patients and operators - to define the individual operator adequate to the needs of the individual case – different scoring systems were developed to predict the probability of successful intervention following transparent assignment of cases and operators. For this purpose, the Japanese Chronic Total Occlusion (J-CTO) score was introduced in 2011, combining several parameters of a CTO including the degree of calcification of the lesion, bending > 45° in the CTO segment or at the entry, blunt proximal cap, length of occluded segment (>20 mm) and a previously failed recanalization attempt. The J-CTO score has been shown to be closely associated with the likelihood of crossing the lesion [8–11]. Since then, it has been considered the gold standard even though the utility in predicting technical success is debatable [12,13]. CTOs were then graded as easy, intermediate, difficult and very difficult (J-CTO Scores of 0, 1, 2 and ≥3 respectively) [14].

This score has some limitations: the overall success rate in the

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original underlying study was only 72 %. Some score data were mainly operator - dependent, and the percentage of retrograde strategies was low [8,11].

Recently Szijgyarto et al. presented the novel CASTLE score which was developed on the basis of the EURO CTO registry and included>20,000 CTO cases between 2008 and 2016 in >50 European centres. The score combined a previous coronary artery bypass graft surgery (CABG), over 70 years of age, a blunt stump morphology, severe tortuosity of the vessel, length of the occlusion and extent of lesion calcification [15]. A CTO was graded to six severity levels 1–6 with one point for each factor. The study showed technical failure increasing from 8% with a CASTLE score of 0 to 1, to 35% with a score≥ 4.

The aim of our study was to compare both scores in predicting technical success in a patient cohort of 463 consecutive patients with at least one CTO.

2. Methods

The present study was designed as an observational retrospective study, including 463 patients undergoing CTO-PCI in one experienced German high volume CTO center between 2015 and 2020. The indication for CTO-PCI was based on current recommendations [16–18] given the presence of clinical symptoms including typical angina pectoris or dyspnea referring to limited exercise capacity and furthermore myocardial viability testing was proven either by evidence of normal wall motion or hypokinesia in the CTO territory assessed by transthoracic echocardiography. In the presence of akinesia in the CTO-territory positive functional ischemia/viability was proven by stress-echocardiography or cardiac magnetic resonance imaging (cMRI) in the territory of the CTO.

The procedures were performed by dual access using bifemoral or radial-femoral. After initial contralateral contrast injections the length of the CTO lesion and the existence and extent of collateral connections was carefully analyzed. The decision to treat patients either by antegrade or retrograde CTO-PCI techniques was based on the operatorś discretion. To prevent thromboembolic complications, heparin was administered intravenously during CTO-PCI guided by regular measurements of the activated clotting time (>300 sec.). The J-CTO score was calculated for all patients, as well as the CASTLE score which was calculated according to the algorithms described by Szijgyarto et al. The study was performed in accordance with the Declaration of Helsinki and the local ethics committee approved this study. In all cases the occluded segment was stented with drug-eluting stents (DES), and postdilatation was performed to optimize stent expansion and apposition. If required, the maneuvers were guided by intravascular ultrasound (IVUS) to better understand the proximal cap anatomy identifying the exact entry point of the CTO, as well as the extent of disease in the distal reference vessel. After CTO-PCI, a dual antiplatelet therapy consisting of 100 mg of aspirin once daily indefinitely and 75 mg of clopidogrel once daily for at least 6 months was ordered. The primary endpoint was technical success, defined as a successful recanalization of the CTO with a residual stenosis <30% and restoration of thrombolysis in myocardial infarction (TIMI)-flow grade 3. A composite safety endpoint including in-hospital death, vascular complications which combines access site hematoma, retroperitoneal hematoma, minor or major bleeding or arterial dissection and/or occlusion, coronary perforation which needed treatment by pericardial puncture, *peri*-interventional myocardial infarction (MI) which was defined as occurrence cardiac troponin in the blood of a patient who also exhibits signs or symptoms of MI, stroke, contrast induced nephropathy defined as absolute (≥0.5 mg/dl) or relative increase (≥25%) in serum creatinine at 48 h after exposure of a contrast agent and emergency CABG was evaluated for every patient. Furthermore, a 30 day follow-up by a telephone interview was performed. Here improvement of clinical symptoms and re-hospitalization was evaluated as well.

2.1. Statistical analysis

The analysis was performed using SAS 9.4 for Windows and STATA 11.0. The distribution of variables is described with counts and percentages for categorical and with mean and standard deviation for continuous variables. Normality of the data was tested using the Shapiro-Wilk Test. In case of rejected normality the Kruskal-Wallis test was used to compare the data of more than two independent samples. Otherweise the F test was chosen. To compare the frequency distribution of a variable in independent samples Fisher's exact test was used. To quantify the dependency of the two scores Spearman rank correlation coefficient was calculated. The diagnostic quality of the two scores was examined and compared with ROC analyses. All tests were calculated two-sided. The analysis is of exploratory character. Therefore, the p-values are interpreted purely descriptively.

3. Results

A total of 463 patients were included between 2015 and 2020. The majority of the patients were male (75.4 %) and the mean age was 63.8 years (±10.5 years). Baseline characteristics are presented in Table 1.

The patients of our cohort suffered from a high cardiovascular risk profile (Table 1). Furthermore, history of CABG was reported in 11.2% and a high number of patients with a prior MI was noticed with 43.0%. 121 patients (26.1 %) were older than 70 years and 15.6% of the patients in this study had a failed CTO recanalization attempt before.

Table 2 summarizes the angiographic parameters of our cohort. While the majority of the patients had a multivessel coronary artery disease (CAD), the target CTO vessel was predominantly the right coronary artery (RCA). In almost 60% of the patients we found an entirely retrograde collateralization and a collateral channel (CC) connection grade 1. In most of the cases we saw a slight vessel tortuosity, a mild and moderate vessel calcification and a blunt stump morphology.

Table 3 describes the procedural characteristics. In approximately 75% a primarily antegrade approach was successful, while in 10.6% a primarily retrograde approach and in 12.7% an ante-retrograde approach was chosen. The overall technical success rate was 83.2% and the overall complication rate was low (5.83%) without any intrahospital death. Vascular complications such as a local hematoma at

Table 1
Baseline characteristics.

	(n = 463)
Age (in years)	63.8 ± 10.5
Age > 70 years	26.1% (121)
Hypertension	80.3% (372)
Diabetes	32.2% (149)
Male Gender	75.4% (349)
Smoking	57.6% (267)
COPD	2.2% (10)
BMI	29.1 ± 5.0
Hyperlipidaemia	84.9% (393)
LDL Cholesterol > 100 mg/dl	67.8% (314)
PAD	7.8% (36)
Family history for CAD	28.7% (113)
Chronic kidney disease	10.8% (50)
Prior MI	43.0% (199)
Prior CABG	11.2% (52)
Prior Stroke	1.1% (5)
Prior PCI	47.9% (222)
Previous CTO PCI attempts	15.6% (72)
Ejection fraction	
<35%	5.2% (24)
>50%	80.1% (371)
35–50%	14.7% (68)

BMI:body mass index; CABG:coronary artery bypass graft; COPD: chronical obstructive pulmonary disease; CTO:chronic total occlusion; LDL:low density lipoprotein; MI:myocardial infarction; PAD: peripheral artery disease; PCI:percutaneous coronary intervention.

Table 2
Angiographic characteristics.

	(n = 463)
Coronary artery disease	
1 vessel	37.4% (173)
2 vessel	30.9% (143)
3 vessel	31.7% (147)
CTO target vessel	
LAD	27.2% (126)
LCX	15.8% (73)
RCA	57.0% (264)
CTO location	
Ostial	9.1% (42)
Proximal	26.6% (123)
Mid	57.0% (264)
Distal	8.2% (38)
In-Stent CTO	13.2% (61)
CTO length > 20 mm	33.5% (155)
Bifurcation involvement	15.1% (70)
Collateral fillings	
Retrograde	59.2% (274)
Ipsilateral	24.4% (113)
Both	17.1% (79)
Collateral circulation	
CC0	23.5% (109)
CC1	63.1% (292)
CC2	14.7% (68)
CTO bending	
<45°	7.1% (33)
>45°	92.9% (430)
Vessel calcification	
Mild	73.4% (340)
Moderate	13.8% (64)
Severe	12.7% (59)
Stump classification	
No stump	26.6% (123)
Blunt stump	55.1% (255)
Tapered stump	18.4% (85)
Sidebranch < 3 mm proximal to CTO	2.2% (10)
Distal opacification	
Faint	94.4% (437)
Good	5.6% (26)
Distal vessel	
Severe disease	63.1% (290)
Minimal disease	37.4% (173)

CTO:chronic total occlusion; LAD:left anterior descending; LCX:left circumflex; RCA:right coronary artery; CC:collateral channel.

Table 3
Procedural and Follow-up characteristics.

	(n = 463)
Approach	
Primarily antegrade	76.5% (354)
Primarily retrograde	10.6% (49)
Ante-retrograde	12.7% (59)
Retro-antegrade	0.2% (1)
Procedural time (in min)*	90 [60–128]
Fluoroscopic time (in min)*	26 [25–42]
Contrast medium (in ml)*	180 [130–250]
Dose area product (in cGY*cm^2)*	5698 [3566–9854]
Number DES*	2 [1–3]
Total length DES (in mm)*	56 [32–80]
Diameter of DES (in mm)*	3 [2.5–3.5]
Periprocedural Complications	
MI	0.4% (2)
Stroke	0.2% (1)
Vascular	1.5% (7)
Emergency CABG	0.2% (1)
CIN	1.3% (6)
Coronary perforation	2.2% (10)
In Hospital death	0
30 Days Follow – Up	
Stroke	0.2% (1)
Re-Hospitalization	0.4% (2)
Vascular	0.2% (1)
Symptoms improved	82.5% (382)
CIN	1.5% (7)
Stent thrombosis	0.2% (1)
Technical success rate	83.2% (385)

CABG:coronary artery bypass graft; CIN:contrast medium induced nephropathy; DES:drug eluting stent; MI:myocardial infarction.
* Median [Q1-Q3].

the puncture side were rare (1.5%).

Any perforation including collateral connections were reported in 2.2% of cases. Clinically relevant perforations, which needed pericardiocentesis occurred in 4 cases (0.86%) and 6 patients suffered from contrast induced nephropathy. The 30 day follow – up demonstrated a good clinical result with low proportion of re-hospitalization (0.4%) and moreover an improvement of clinical symptoms in >83% of patients.

The overall mean J-CTO score was 2.84 ± 1.0 and the mean CASTLE score was 2.23 ± 1.1. The bar chart in Fig. 1 demonstrates a linear correlation between the two scores, and the Spearman correlation coefficient was 0.724 ($p < 0.001$). Still, the success rate was lower for higher values of both scores as presented in Figs. 2a and 2b. To evaluate the discriminatory performance of the J-CTO- and CASTLE-score Receiver operating characteristic (ROC) analysis was performed (Fig. 3a) predicting the technical outcome: CASTLE score AUC 0.668, 95% CI: 0.606–0.730, p = 0.324; J-CTO score AUC 0.692, 95% CI: 0.631–0.752, p = 0.324; comparison of AUCs: p = 0.324. Those findings were even consistent in more complex procedures CASTLE Score ≥ 4 and J-CTO score ≥ 3: CASTLE Score AUC 0.514, 95% CI: 0.409–0.619, p = 0.211; J-CTO score AUC 0.617, 95% CI: 0.493–0.741, p = 0.211; Comparison of AUCs: p = 0.211.

A significant difference was obvious in the ROC curve analysis, showing a higher discriminatory performance for the CASTLE score than for the J-CTO score in the post-CABG collective (n = 52) (CASTLE score

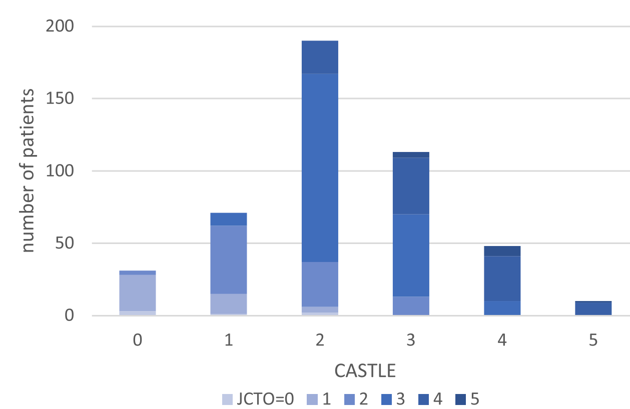

Fig. 1. Relationship of the two scores depending on the different values.

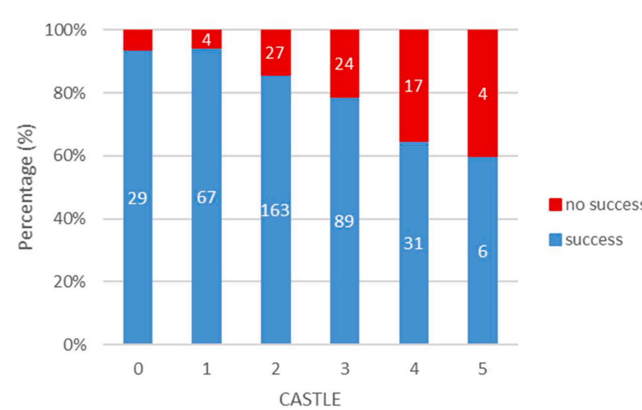

Fig. 2a. Success rates of the CASTLE score depending of the different values.

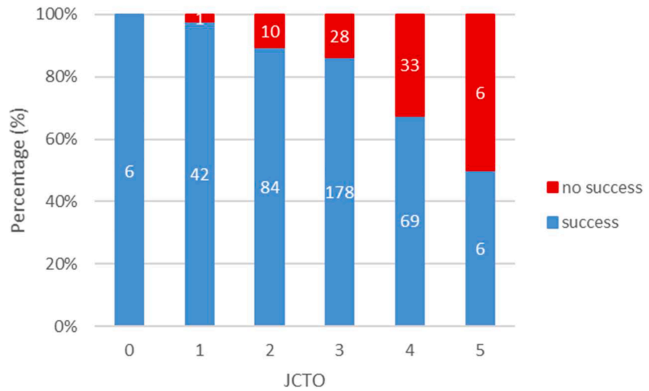

Fig. 2b. Success rates of the J-CTO score depending of the different values.

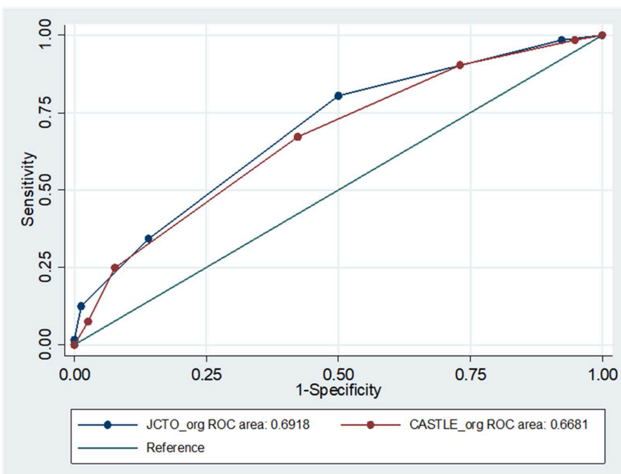

Fig. 3a. ROC curve for success prediction for both scores in all patients.

AUC 0.789, 95% CI: 0.658–0.919, p = 0.080; J-CTO score AUC 0.705, 95% CI: 0.569–0.847, p = 0.080; comparison of AUCs: p = 0.080) (Fig. 3b). This finding is even more evident in more complex cases with a J-CTO score > 3 and CASTLE score > 4 with a p-value of 0.055.

Furthermore, as presented in Tables 4 and 5, we demonstrated that increasing score values are accompanied by a longer examination and fluoroscopy time, more contrast medium and a higher dose area product

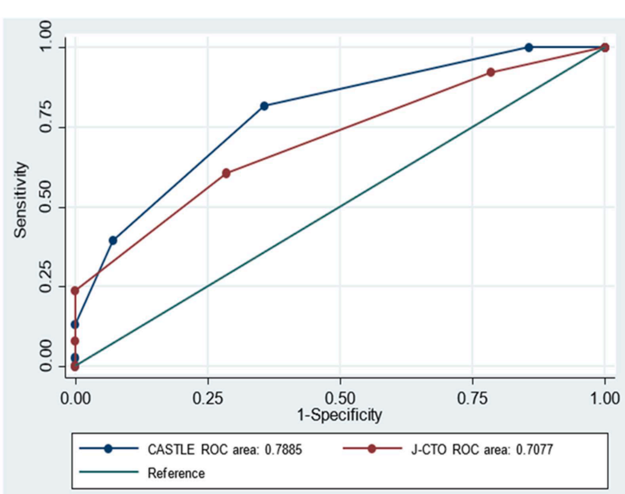

Fig. 3b. ROC curve for success prediction for both scores in CABG patients.

Table 4
Metric periprocedural variables in dependency of the J-CTO score.

	J-CTO	n	Median [Q1-Q3]	p-value*
Procedural time (in min)	0, 1	49	59 [45–62]	<0.001
	2	94	64 [49–109]	
	3	206	90 [63–120]	
	4,5	114	132 [98–180]	
Fluoroscopic time (in min)	0, 1	49	15 [11–22]	<0.001
	2	94	18 [12–32]	
	3	206	25 [16–38]	
	4,5	114	43 [30–62]	
Contrast medium (in ml)	0, 1	49	120 [100–180]	<0.001
	2	94	150 [110–200]	
	3	206	190 [150–250]	
	4, 5	114	200 [150–250]	
Dose area product (in CGY*cm^2)	0, 1	49	3597 [2361–5716]	<0.001
	2	94	4690 [3127–7005]	
	3	206	5415 [3566–9100]	
	4, 5	114	9615 [5796–14612]	

CTO:chronic total occlusion.
* p-value of Kruskal-Wallis test.

Table 5
Metric periprocedural variables in dependency of the CASTLE score.

	CASTLE	n	Median [Q1-Q3]	p-value*
Procedural time (in min)	0, 1	102	60 [47–83]	<0.001
	2	190	90 [63–122]	
	3	113	98 [70–155]	
	>4	58	125 [90–180]	
Fluoroscopic time (in min)	0, 1	102	16 [12–27]	<0.001
	2	190	25 [16–40]	
	3	113	33 [19–47]	
	> 4	58	42 [28–62]	
Contrast medium (in ml)	0, 1	102	150 [100–200]	<0.001
	2	190	180 [140–250]	
	3	113	200 [150–250]	
	> 4	58	200 [150–250]	
Dose area product (in CGY* cm^2)	0, 1	102	4267 [2683–6484]	<0.001
	2	190	5609 [3566–10392]	
	3	113	6796 [3651–10444]	
	> 4	58	8610 [5676–13526]	

* p-value of Kruskal-Wallis test.

(DAP).

4. Discussion

Several studies have underlined the importance of patients' selection for CTO PCI. Furthermore, we learned that patient and operator related factors should be considered when a complex CTO lesion has to be treated [19,20]. Established scores, that are able to predict the success of CTO recanalization and to select appropriate candidates and specialist centers for a recanalization attempt, should represent a key issue to achieve optimal procedural and better long-term outcome [21]. In the past years different scoring systems have been introduced. Identifying the optimal score for predicting success, based on different clinical and anatomical scenarios, remains challenging.

Opolski et al. developed the CT - Rector score, which includes two clinical and four anatomical coronary computed tomography angiography (CCTA) based predictors, for successful lesion crossing within 30 min. CCTA data include multiple occlusions, blunt stump, bending, and severe calcification, clinical data consider reattempted PCI CTO and occlusion duration ≥12 months or unknown. The CT-Rector Score is a solid non-invasive prediction tool for grading CTO which may help to identify very difficult CTO lesions [11,22,23]. However, in his study retrograde approach was chosen in a limited number of the cases (11%), and the overall success rate was only 62% which does not reflect actual standards and requirements of CTO interventions.

The Progress CTO Score which is based on the hybrid approach, with early changes between strategies to enable CTO crossing in an efficient mode, was presented by Christopoulos et al. in 2016. Four parameters (proximal cap ambiguity, lack of interventional collaterals, left circumflex (LCX) CTO, and moderate/severe tortuosity) were identified to be associated with a failed attempt. On the basis of these four characteristics, an initial strategy and rank order hierarchy for technical approaches were established. Though some of the predictors such as identifying collateral vessels as “interventional collaterals” are based on a highly subjective assessment [11,24,25].

Alessandrino et al. introduced the Clinical and Lesion (CL) related score which was developed on the basis of a prospective single-center study on 1,657 patients. This score includes lesion related variables like the anatomy of the proximal cap, grade of lesion calcification, left anterior descending (LAD) or non-LAD CTO, length (>20 mm) of the lesion and in addition clinical details of the medical history such as history of CABG and history of MI [26]. Our group proved that this score can be used as an important marker to define the interventional strategy in patients with CTO and to select the appropriate operator [11].

The ORA score by Galassi et al. included an ostial location, Rentrop collateral filling grade, and age. This model demonstrated satisfactory calibration and discrimination for predicting technical failure using both antegrade and retrograde CTO techniques, and categorized CTO procedures into four groups with increased difficulty and reduced likelihood of success [27]. However, only a single CTO-dedicated operator was involved in this early single center study between 2005 and 2014.

The widely adopted, most commonly used J-CTO score was derived from 465 patients, treated with antegrade approach between 2006 and 2007, with a primary endpoint of successful guidewire crossing within in 30 min, which was achieved in 48% of the cases [8].

In a large meta-analysis by Karatasakis et al. various scoring systems were evaluated between 2012 and 2016. They concluded that the CL-, J-CTO- and PROGRESS CTO-score perform moderately in predicting technical outcome of CTO PCI, with better performance for antegrade-only procedures [30].

The recently reported CASTLE score, a novel CTO PCI success prediction scoring system, has the advantage of a large unselected contemporary population of>20,000 cases. Beside the fact of four anatomical predictors, which are almost similar to the J-CTO score, this scoring system provides two additional clinical predictors (CABG, age > 70) for success [16]. Kalogeropoulos et al. showed that the CASTLE score was superior in predicting successful recanalizations in more complex CTO lesions [29]. There were several important differences in their outcomes compared to our study. First of all, the overall success rate was lower (78%), as well as the overall mean scores (J-CTO: 1.9 ± 1.2; CASTLE: 1.8 ± 1.2).

Our study proves an equal overall predictive performance of the recently presented CASTLE score compared with the gold standard, the J-CTO score, in identifying CTO lesions with a likelihood for successful recanalization, in an unselected contemporary population. We showed that the CASTLE score seems to be superior in CTO patients after CABG. We know from several studies that this cohort of patients is very challenging [31]. Recently Brilakis et al. demonstrated in a large meta-analysis that patients undergoing PCI for CTO lesions have poorer outcomes and more complex procedures if they have previously undergone CABG surgery [32].

In most scoring systems, patients with higher lesion complexity based on the descripted scores systems, have lower probability for successful CTO revascularization attempt. Adhikari et al. concluded that in those patients, CABG should be preferred to avoid unnecessary radiation, or refer to a high-volume CTO PCI center where different approaches and adjuvant modalities are utilized and highly experienced operators perform CTO PCI [33]. Alternatively, Scott et al. emphasized the importance of proctorship for complex cases. Different techniques such as retrograde and antegrade dissection re-entry approach should be trained until the operator has gained competency in these techniques [34].

As our findings confirmed that higher grades of the J-CTO score and the CASTLE score are associated with higher levels of parameters such as radiation exposure, contrast volumes, procedural and fluoroscopy times in accordance with previous data [28,29], and lower success rates. The utilization of both scores may be very useful in our daily clinical practice mainly to select consecutive patients and attribute them either to high volume CTO operators and experts or to less experience interventionalist. A preselection of CTO patients, based on anatomical and clinical scores may facilitate our ultimate goal to achieve high revascularization rates at low complication levels with an equal distribution of personal resources in our catheterization laboratories. We believe that widely accepted and validated scores like the CASTLE score are very helpful in daily practice and we presume they can support interventional cardiologists in their treatment decision for improving patients’ outcomes.

4.1. Study limitations

The present study is a retrospective analysis and all data are collected from a single center. The results of this study may have been influenced by selection criteria, bias on operator’s experience, and varying techniques used by the two involved operators. Another limitation may be that the matched and un-matched data used in this study were already collected. Thus, the analysis represents an observational character only. Two analysts calculated the scores retrospectively together.

5. Conclusions

The new developed CASTLE score can be calculated very easily parallel to the well-established J-CTO score and showed a similar performance in predicting CTO PCI success. The additional implementation of the CASTLE score might improve the preselection of complex CTO patients to assign them to more experience centers and operators, resulting in a better clinical outcome.

We showed for the first time a higher discriminatory performance for the CASTLE score than for the J-CTO score in the post-CABG collective.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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