Circulation: Cardiovascular Interventions

ORIGINAL ARTICLE

Sustained Mechanical Aspiration Thrombectomy for High Thrombus Burden Coronary Vessel Occlusion: The Multicenter CHEETAH Study

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BACKGROUND: Poor myocardial reperfusion due to distal embolization and microvascular obstruction after percutaneous coronary intervention is associated with increased risk of morbidity and mortality. Prior trials have not shown a clear benefit of routine manual aspiration thrombectomy. Sustained mechanical aspiration may mitigate this risk and improve outcomes. The objective of this study is to evaluate sustained mechanical aspiration thrombectomy before percutaneous coronary intervention in high thrombus burden acute coronary syndrome patients.

METHODS: This prospective study evaluated the Indigo CAT RX Aspiration System (Penumbra Inc, Alameda CA) for sustained mechanical aspiration thrombectomy before percutaneous coronary intervention at 25 hospitals across the USA. Adults presenting within 12 hours of symptom onset with high thrombus burden and target lesion(s) located in a native coronary artery were eligible. The primary end point was a composite of cardiovascular death, recurrent myocardial infarction, cardiogenic shock, or new or worsening New York Heart Association class IV heart failure within 30 days. Secondary end points included Thrombolysis in Myocardial Infarction thrombus grade, Thrombolysis in Myocardial Infarction flow, myocardial blush grade, stroke, and device-related serious adverse events.

RESULTS: From August 2019 through December 2020, a total of 400 patients were enrolled (mean age 60.4 years, 76.25% male). The primary composite end point rate was 3.60% (14/389 [95% CI, 2.0–6.0%]). Rate of stroke within 30 days was 0.77%. Final rates of Thrombolysis in Myocardial Infarction thrombus grade 0, Thrombolysis in Myocardial Infarction flow 3, and myocardial blush grade 3 were 99.50%, 97.50%, and 99.75%, respectively. No device-related serious adverse events occurred.

CONCLUSIONS: Sustained mechanical aspiration before percutaneous coronary intervention in high thrombus burden acute coronary syndrome patients was safe and was associated with high rates of thrombus removal, flow restoration, and normal myocardial perfusion on final angiography.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT03957473.

GRAPHIC ABSTRACT: A graphic abstract is available for this article.

Key Words: acute coronary syndrome ■ myocardial infarction ■ percutaneous coronary intervention

Acute myocardial infarction (MI), typically resulting from coronary plaque rupture and thrombus formation and vessel occlusion, is a leading cause of morbidity and mortality.[1] Treatment focuses on minimizing infarct size by reopening the impacted artery and restoring myocardial perfusion.[1] While percutaneous coronary intervention (PCI) is an established treatment option and can reliably re-establish flow, it can

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WHAT IS KNOWN

- While percutaneous coronary intervention is an established treatment option for high thrombus burden patients and can reliably re-establish flow, it can also cause distal embolization, resulting in persistent microvascular obstruction and poor myocardial perfusion.
- Prior trials have not shown a clear cardiovascular benefit of routine manual aspiration thrombectomy and may also have a higher risk of stroke.

WHAT THE STUDY ADDS

- The sustained mechanical aspiration thrombectomy system studied in this study represents a major technological advancement over the syringe-based manual aspiration catheters used historically.
- Based on the encouraging results of this study, future randomized controlled trials may demonstrate the benefit of mechanical aspiration thrombectomy in high thwrombus burden percutaneous coronary intervention.

Nonstandard Abbreviations and Acronyms

ACS	acute coronary syndrome
MBG	myocardial blush grade
MI	myocardial infarction
PCI	percutaneous coronary intervention
STEMI	ST-segment–elevation myocardial infarction
TIMI	Thrombolysis in Myocardial Infarction

also cause distal embolization, resulting in persistent microvascular obstruction and poor myocardial perfusion.[2–5] Poor myocardial perfusion after PCI is associated with worse left ventricular functional recovery and increased long-term mortality.[5–7] By removing thrombotic material, aspiration thrombectomy before PCI may reduce the risk of distal embolization and improve myocardial perfusion. Key outcomes from historical randomized thrombectomy trials that reported myocardial blush grade (MBG) are available in Table S1. Initial randomized trials found that manual aspiration thrombectomy before PCI improved myocardial perfusion and clinical outcomes compared to PCI alone.[8,9] However, subsequent trials did not find the same benefits, causing uncertainty around the utility of routine aspiration.[10–15] The TOTAL trial (Randomized Trial of Routine Aspiration Thrombectomy With PCI Versus PCI Alone in Patients With STEMI Undergoing Primary PCI) found that routine manual aspiration thrombectomy before PCI did not significantly reduce the rate of the primary composite safety end point compared to PCI alone (6.9% versus 7.0%; *P*=0.86).[12] Additionally, a meta-analysis of large randomized trials comparing aspiration thrombectomy and PCI alone found that routine manual aspiration thrombectomy did not improve clinical outcomes.[15] However, in the high thrombus burden subgroup, manual aspiration thrombectomy was associated with reduced cardiovascular death but increased stroke or transient ischemic attack.[15] For select cardiac populations, particularly those with high thrombus burden, the role of aspiration thrombectomy is still a matter of active debate.[16]

The predominant technology used in prior trials was syringe-based manual aspiration. Manual aspiration suffers from decreasing aspiration force as the syringe fills with fluid and requires the operator to exchange syringes during the procedure to maintain suction.[17] By comparison, sustained mechanical aspiration with a dedicated vacuum pump delivers constant aspiration force while thrombectomy is being performed.[17] Sustained mechanical aspiration is well established and commonly used for thrombus removal in the neurovasculature.[18] Applying this innovation to the coronary vasculature may reduce the risk of microvascular obstruction associated with PCI and improve outcomes.

We evaluate the initial safety and performance of sustained mechanical aspiration using the Indigo CAT RX Aspiration System (Penumbra Inc, Alameda, CA) before PCI in patients with acute coronary vessel occlusion and high thrombus burden. Compared with prior coronary aspiration catheters, the CAT RX aspiration catheter has a softer distal tip, a larger aspiration port and lumen, and the ability to provide continuous mechanical aspiration.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Design

CHEETAH (A Prospective, Multicenter Study to Evaluate the Safety and Performance of the CAT RX Aspiration Catheter in Patients With a High Thrombus Burden Acute Coronary Vessel Occlusion) was a single-arm, postmarket registry study that enrolled patients from August 2019 through December 2020 at 25 hospitals across the United States and was designed to assess the feasibility of broader utilization of sustained mechanical aspiration thrombectomy. Patients were followed for 180 days or to outcome (ie, withdrawal or death), whichever occurred first. Consecutive patients presenting with acute coronary vessel occlusion and high thrombus burden who were referred for PCI were screened. Sites kept a screening log of potential study candidates with reason(s) for exclusion recorded (Table S2). The study was conducted with proper ethical oversight, and each site obtained institutional review board (Listing S1) approval prior to enrolling patients. Inclusion criteria were as follows: age ≥18 years, presenting to treating facility within 12 hours of symptom onset, coronary occlusion with high

thrombus burden (Thrombolysis in Myocardial Infarction [TIMI] thrombus grade 4 or 5 on angiography after the guidewire crossed the target lesion), target lesion located in a native coronary artery, utilization of the Indigo CAT RX Aspiration System prior to PCI, and informed consent obtained from either the patient or a legally authorized representative. Due to the nature and severity of acute MI, informed consent could be obtained up to 2 calendar days postprocedure, but prior to discharge. The choice of aspiration frontline or percutaneous transluminal coronary angioplasty first was based on the operator discretion. Exclusion criteria were as follows: new onset of stroke symptoms and National Institutes of Health Stroke Scale score >2 prior to index procedure, treatment with fibrinolytic therapy for index coronary vessel occlusion, life expectancy <6 months due to any comorbidities, patient unwilling or unable to comply with protocol follow-up schedule or based on the Investigator's judgement that the patient was not a good study candidate, participation in another investigational drug or device study that may confound the results of this study, and patient was pregnant.

End Points

The study used previously published end point definitions. The primary end point was major adverse cardiovascular events—a composite of cardiovascular death, recurrent MI, cardiogenic shock, or new or worsening New York Heart Association class IV heart failure within 30 days.[12] Secondary performance end points were final TIMI flow grade,[19] final TIMI thrombus grade,[20] MBG,[5] distal embolization rate, and stent thrombosis at 180 days. Secondary safety end points were incidence of device-related serious adverse events, stroke and major bleeding within 30 days, and all-cause mortality, cardiovascular death, recurrent MI, cardiogenic shock, and class IV heart failure within 180 days. Stroke was defined as the presence of new focal neurologic deficits thought to be vascular in origin, with signs or symptoms lasting >24 hours. Stroke severity was categorized as major if there was an increase of ≥4 points on the National Institutes of Health Stroke Scale at 24 hours after stroke onset; otherwise, stroke severity was considered minor. Adverse events with probable or definite relationship to the Indigo CAT RX Aspiration System, as adjudicated by the independent medical reviewer, were considered device related. Detailed definitions are available in Table S3. Sites entered data using the InForm Electronic Data Capture System (Oracle, Austin, TX). The sponsor implemented risk-based monitoring to ensure data consistency and protocol adherence.

Study Oversight Committees

The independent medical reviewer and members of the independent core laboratory were not involved with patient enrollment or care. The independent medical reviewer reviewed and adjudicated adverse events for relationship to device and study end points. The core laboratory used previously published grading methods to assess cardiac imaging for TIMI thrombus grade, TIMI flow grade, MBG, and distal embolization. Assessments were performed for TIMI thrombus[20] and TIMI flow grades[19] according to the standard methodology and for MBG[5] using the best available angiographic images.

Role of the Sponsor

The sponsor, Penumbra Inc (Alameda, CA), performed database setup, site and data monitoring, statistical analysis, and manuscript editorial support. The authors were involved in study design, data collection, and the writing of the manuscript. Any data interpretation and conclusions contained in this article are those of the authors.

Device and Procedure

The Indigo CAT RX Aspiration System is a sustained mechanical aspiration thrombectomy system composed of the CAT RX aspiration catheter, a Penumbra aspiration pump (Penumbra ENGINE or Pump MAX), and associated tubing with flow switch to activate aspiration. It received FDA clearance on May 2017 for the removal of fresh, soft emboli and thrombi from vessels in the coronary and peripheral vasculature. The CAT RX aspiration catheter (Figure 1) is a rapid exchange catheter compatible with a 0.014″ guidewire and a 6F guide catheter. The pump provides continuous vacuum pressure of up to −29 in Hg.

Preparation for treatment was performed per site standard-of-care (intravascular imaging used per operator discretion; see Table S4). Thrombectomy procedures were performed as follows. With the flow switch in the off position, the Penumbra aspiration pump was turned on and allowed to reach maximum suction. The CAT RX aspiration catheter was flushed prior to the procedure. After the initial angiogram and crossing the lesion with the guidewire, the aspiration catheter was advanced through the guide catheter and navigated to the lesion. Upon exiting the distal end of the guide catheter, the flow switch was turned on, allowing for sustained mechanical aspiration to be applied through the aspiration catheter as it was advanced to or across the lesion. After a period of time per operator discretion, the catheter was withdrawn out of the body under continuous aspiration and the flow switch was not turned off until the aspiration catheter had exited the Touhy-Borst valve. Estimated blood loss is reported based on the estimate of blood volume in the canister. Additionally, thrombus may completely occlude and become lodged in the catheter while under continuous aspiration, resulting in no flow and minimal blood loss. Prior to readvancing the aspiration catheter, if deemed necessary by the operator, the catheter was flushed with saline to clear any blockage and avoid thrombus reintroduction into the coronary arteries. Postthrombectomy, PCI was performed.

Statistical Methods

All CIs presented are 2-sided. All statistical tests are 2-tailed with a significance level of 0.05. Descriptive statistics are provided. Analyses were conducted using SAS (SAS Institute, Cary, NC). The sample size calculations assumed that 6.1% (22/360) of the study subjects would experience a primary safety event, comparable to 6.1% (272/4454) of the TOTAL trial's high thrombus burden subset.[21] Based on this binomial analysis with a noninferiority margin of 10%, a sample size of 360 Indigo CAT RX Aspiration System subjects would have a 99% power with a 1-sided alpha of 0.025. The sample size was adjusted to 400 subjects to account for up to 10% attrition.

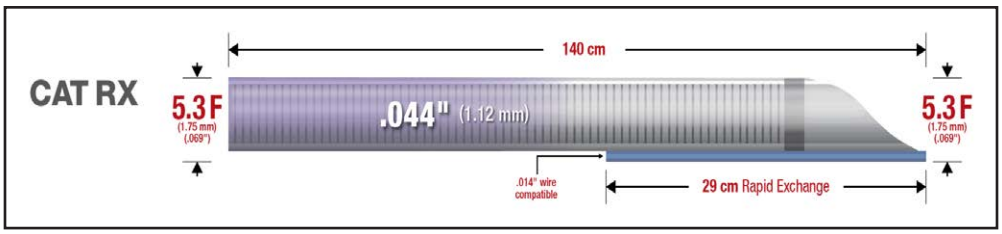

Figure 1. CAT RX aspiration catheter.
CAT RX aspiration catheter dimensions.

RESULTS

Between August 2019 and December 2020, of the 1380 patients screened, 400 were enrolled. A patient flow diagram is detailed in Figure S1. The most common reason for screen failure was for inadequate thrombus burden at coronary angiography (39.59%, 388/980). Study completion rate, including patients who died during follow-up, was 92.50% (370/400). Five withdrew consent, one was withdrawn by a study investigator, and 24 were lost to follow-up. Informed consent was obtained preprocedure in 20.25% (81/400) of cases and postprocedure in 79.75% (319/400) of cases; there were no significant differences in outcomes between these groups (Table S5). Patient demographics are detailed in Table 1. The patient population (mean age 60.4±12.2 years, 23.75% female, 85.50% White patients) had a medical history typical of acute MI patients (64.50% hypertension, 48.50% dyslipidemia, and 20.00% with prior PCI). The distributions of heart failure severity are shown in Figure 2. Index event and procedural information are detailed in Table 2. The index event was ST-segment–elevation myocardial infarction (STEMI) for 87.50% of patients and non–ST-segment–elevation myocardial infarction for the remaining 12.50%. The most common target lesion locations were the right coronary artery (49.75%) and the left anterior descending artery (37.00%). Multiple target lesion locations were present in 0.75%. After guidewire crossing, all patients, except one, had TIMI thrombus grades 4 or 5 by physician visual estimate. Mean door-to-device time, including time required for device setup, for STEMI patients was 59.4 minutes. The median number of passes with the CAT RX aspiration catheter was one and the median aspiration time was 69 seconds. Operators reported that CAT RX enhanced visualization of the target lesion in 94.72% of cases and the median estimated blood loss with aspiration was 19 mL.

Safety End Points

The safety end points are available in Table 3. The primary composite major adverse cardiovascular events rate within 30 days was 3.60% (95% CI, 2.0–6.0%), compared with the historical rate of 6.1% ($P_{noninferiority}$<0.001). No transient ischemic attacks were reported within 30 days. Stroke within 30 days occurred in 3 patients (0.77% [95% CI, 0.2–2.2%]) and was confirmed by neuroimaging. One major stroke occurred at day 20 postprocedure. One major stroke was discovered at day 3 postprocedure by magnetic resonance imaging, although symptoms consistent with a neurovascular event were present before enrollment. One minor stroke occurred at day 2 postprocedure in a patient requiring multiple guide catheter exchanges before target vessel access could be obtained. Cardiovascular death within 30 days occurred in 2 patients (0.51% [95% CI, 0.1–1.8%]). Both were in cardiogenic shock and neither were device related. Four patients experienced major bleeding within 30 days (1.03% [95% CI, 0.3–2.6%]). All were related to the procedure, but

Table 1. Patient Demographics

	All patients (N=400)
Age, y; mean (SD)	60.4 (12.2) (n=400)
>18, <65	63.75% (255/400)
≥65	36.25% (145/400)
Sex, female; % (n/N)	23.75% (95/400)
Race; % (n/N)*	
American Indian or Alaska Native	0.50% (2/400)
Asian	3.00% (12/400)
Black or African American	8.00% (32/400)
Native Hawaiian or Other Pacific Islander	0.75% (3/400)
White	85.50% (342/400)
Not reported	2.50% (10/400)
Ethnicity, Hispanic or Latino; % (n/N)	3.50% (14/400)
Medical history; % (n/N)	
Cardiogenic shock	2.50% (10/400)
Diabetes	23.50% (94/400)
Dyslipidemia	48.50% (194/400)
Hypertension	64.50% (258/400)
Myocardial infarction	16.25% (65/400)
Stroke, ischemic	3.00% (12/400)
Stroke, hemorrhagic	1.00% (4/400)
Prior CABG	2.00% (8/400)
Prior PCI	20.00% (80/400)
Family history of cardiovascular disease; % (n/N)	41.75% (167/400)
Social history of tobacco use (current or former); % (n/N)	57.50% (230/400)

CABG indicates coronary artery bypass graft; and PCI, percutaneous coronary intervention.
*Multiple responses are allowed for each patient.

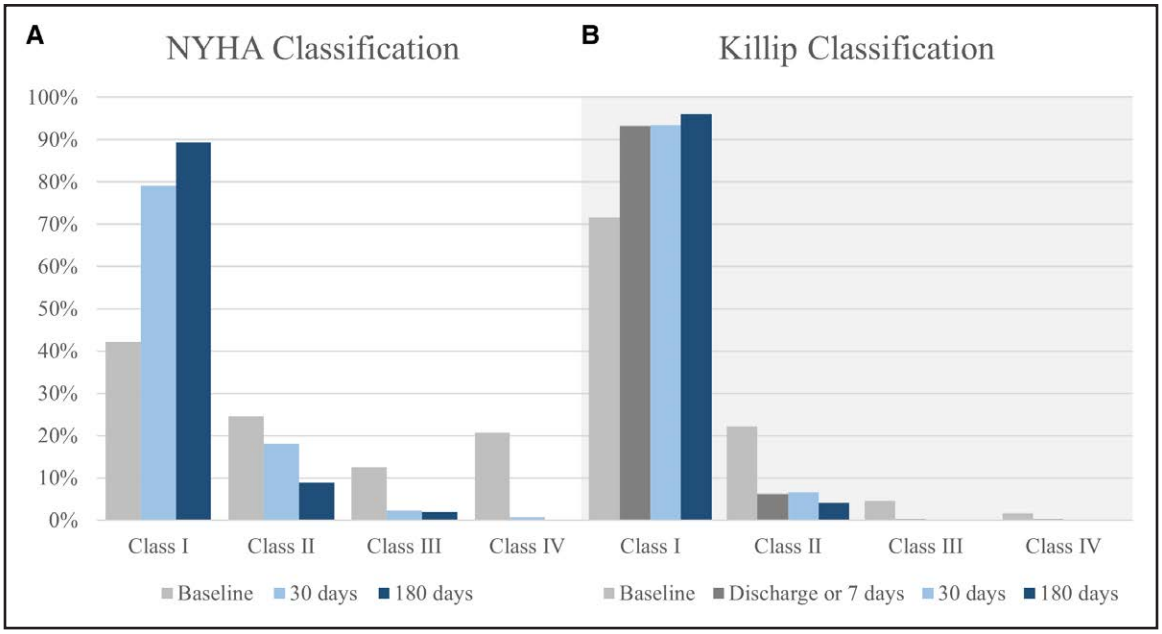

Figure 2. Heart failure classifications.
A, New York Heart Association (NYHA) and (**B**) Killip classifications of heart failure.

not attributed to the device. Three patients had access-site complications (2 retroperitoneal hematomas and 1 access-site bleeding) and 1 patient had a progressive hemoglobin drop in the setting of a chronic gastrointestinal bleed on antiplatelets. There were no device-related serious adverse events. Rate of New York Heart Association class IV heart failure within 180 days was 1.08% (95% CI, 0.3–2.7%) and the rate of cardiovascular death within 180 days was 1.08% (95% CI, 0.3–2.7%). Additionally, no significant differences in outcomes were identified in a comparison of the STEMI and non–ST-segment–elevation myocardial infarction subgroups (Table S6).

Performance End Points and Angiographic Assessments

The performance end points and distributions of angiographic outcomes, as assessed by the core laboratory, are shown in Table 3 and Figures 3 and 4. Distal embolization rate postprocedure was 0.75% (95% CI, 0.2–2.2%). Rate of stent thrombosis within 180 days was 2.43% (95% CI, 1.1–4.6%). On final angiography, TIMI thrombus grade 0 was achieved in 99.50% (95% CI, 98.2–99.9%) of cases, TIMI flow grade 3 in 97.50% (95% CI, 95.5–98.8%), and MBG 3 in 99.75% (95% CI, 98.6–100.0%). An example case is presented in Figure 5.

Serial Assessments of the Signs and Symptoms of Heart Failure

At baseline, 28.46% (105/369) of patients had signs of heart failure on physical examination (Killip class II through IV), and by discharge after the procedure, this decreased to 6.74% (24/356). At baseline, 57.82% (207/358) of patients reported symptoms of heart failure categorized as New York Heart Association class II through IV; this decreased to 10.74% (35/326) at 180 days. Distributions of Killip and New York Heart Association Classes at various time points are shown in Figure 2.

DISCUSSION

Summary of the Results

In this initial study, selective sustained mechanical aspiration thrombectomy in high thrombus burden acute coronary syndrome (ACS) patients was suggested to be safe and associated with a low major adverse cardiovascular events rate of 3.60% (95% CI, 2.0–6.0%). The final TIMI thrombus grade 0 (99.50%) and final TIMI flow grade 3 (97.50%) demonstrate excellent thrombus debulking and outcome with regard to the epicardial arteries. While prior trials found that aspiration thrombectomy improves tissue level perfusion over PCI alone (OR, 3.04 [95% CI, 1.74–5.78]), TIMI myocardial perfusion grade 3 has historically only been achieved in 47.6% (range 26.9–87.8%) of patients treated with any thrombectomy device and 52.2% (range, 35.8–87.8%) with aspiration thrombectomy.[22] The rate of MBG 3 immediately after CAT RX treatment (45.69%) was similar to final MBG 3 in previous trials, including those using manual aspiration, but in CHEETAH, the rate of final MBG 3 (99.75%) was remarkably high, perhaps related to more efficient and reliable clot removal using sustained thrombectomy that resulted in normalized microvascular function after the subsequent PCI.[8,12,23–26] The study

Table 2. Index Event and Procedure Characteristics

	All patients (N=400)
Index event diagnosis; % (n/N)	
STEMI	87.50% (350/400)
NSTEMI	12.50% (50/400)
Onset-to-treatment-facility-arrival time, h; mean (SD)*	2.7 (2.82) (n=389)
Door-to-device time, min; mean (SD)†	59.4 (43.4) (n=349)
Door-to-reperfusion time, min; mean (SD)†	63.9 (45.3) (n=339)
Primary target lesion treatment location(s); % (n/N)‡	
Right coronary artery	49.75% (199/400)
Left main	0.50% (2/400)
Left anterior descending	37.00% (148/400)
Ramus intermedius	0.50% (2/400)
Left circumflex	13.00% (52/400)
Lesion classification according to ACC/AHA guidelines; % (n/N)	
Type A	8.27% (32/387)
Type B	33.59% (130/387)
Type C	58.14% (225/387)
Percent stenosis in target vessel; mean (SD)	99.1 (3.23) (n=400)
Multiple target lesion location; % (n/N)	0.75% (3/400)
Lesion length, mm; mean (SD)	24.0 (14.27) (n=378)
Intravascular imaging use; % (n/N)§	19.00% (76/400)
ACT value, s; mean (SD)	301.5 (76.30) (n=283)
Glycoprotein IIb/IIIa inhibitor use; % (n/N)	33.25% (133/400)
Total aspiration time with CAT RX, s; median [IQR]	69 [45–124] (n=283)
Number of passes with CAT RX, n; median [IQR]	1 [1–2] (n=396)
Estimated blood loss with aspiration, mL; median [IQR]	19 [10–25] (n=350)
Enhanced visualization of the target lesion post CAT RX; % (n/N)	94.72% (377/398)

ACC indicates American College of Cardiology; ACT, activated clotting time; AHA, American Heart Association; IQR, interquartile range; MI, myocardial infarction; NSTEMI, non–ST-segment–elevation myocardial infarction; and STEMI, ST-segment–elevation myocardial infarction.

*Patients who were admitted prior to symptom onset (ie, in-hospital MI patients) had onset-to-arrival times of 0 min.

†For STEMI patients only.

‡Multiple responses allowed for each patient.

§A total of 68 patients received intravascular ultrasound, 7 received optical coherence tomography, and 1 received both.

Table 3. End Points per IMR

	All patients (N=400)
Primary composite end point (MACE); % (n/N; [95% CI])*	3.60% (14/389; 2.0%, 6.0%)
Cardiovascular death within 30 d	0.51% (2/389; 0.1%, 1.8%)
Recurrent MI within 30 d	1.80% (7/389; 0.7%, 3.7%)
Cardiogenic shock within 30 d	1.80% (7/389; 0.7%, 3.7%)
New or worsening NYHA class IV heart failure within 30 d	0.77% (3/389; 0.2%, 2.2%)
Secondary safety end points; % (n/N; [95% CI])	
Stroke within 30 d†	0.77% (3/389; 0.2%, 2.2%)
Major stroke within 30 d	0.51% (2/389; 0.1%, 1.8%)
Minor stroke within 30 d	0.26% (1/389; 0.0%, 1.4%)
Major bleeding within 30 d‡	1.03% (4/389; 0.3%, 2.6%)
All-cause mortality within 180 d	2.43% (9/370; 1.1%, 4.6%)
Cardiovascular death within 180 d	1.08% (4/370; 0.3%, 2.7%)
Recurrent MI within 180 d	2.70% (10/370; 1.3%, 4.9%)
Cardiogenic shock within 180 d	2.16% (8/370; 0.9%, 4.2%)
Class IV heart failure within 180 d	1.08% (4/370; 0.3%, 2.7%)
Incidence of device-related SAE(s)§	0.00% (0/389; N/A)
Distal embolization rate; % (n/N; [95% CI])‖	0.75% (3/400; 0.2%, 2.2%)
Stent thrombosis within 180 d; % (n/N; [95% CI])	2.43% (9/370; 1.1%, 4.6%)

IMR indicates independent medical reviewer; MACE, major adverse cardiovascular events; MI, myocardial infarction; NYHA, New York Heart Association; and SAE, serious adverse event.

*Denominators exclude patients lost to follow-up or withdrawn.

†All cases of stroke were adjudicated as being unrelated to the device.

‡All cases of major bleeding were adjudicated as being unrelated to the device.

§Device-related events are events that were adjudicated as probably or definitely related to the Indigo CAT RX Aspiration System.

‖Per core laboratory.

criteria focused on patients presenting within 12 hours of symptom onset, in line with guidelines recommending PCI in patients with STEMI and ischemic symptoms for <12 hours to improve survival.[27] Furthermore, this is consistent with the enrollment criteria for the TAPAS (Thrombus Aspiration During Percutaneous Coronary Intervention in Acute Myocardial Infarction) and TOTAL trials.[8,12] It is possible that patients with late presentation (>12 hours) may have different or even less favorable outcomes. This would need to be separately studied. It will be important to validate the CHEETAH results in a larger randomized controlled trial.

Early investigation found that routine manual aspiration reduced distal embolization (9.3% versus 16.8%; P=0.10)[23] and improved, but did not normalize MBG compared with conventional PCI.[8] Subsequent large randomized trials suggested no clinical benefit and an increased stroke risk at 30 days—even in the high thrombus burden subset (HR, 1.90 [95% CI, 1.04–3.48]).[10,12,21] Accordingly, the American College of Cardiology/American Heart Association revascularization guidelines made routine aspiration thrombectomy a class III recommendation and selective and bailout thrombectomy a class IIb recommendation.[16] Mechanical thrombectomy has also not yielded beneficial results historically. In a meta-analysis, mechanical thrombectomy, compared with PCI alone, was associated with higher mortality (5.3% versus 2.8%; P=0.05).[28] It is possible these studies simply

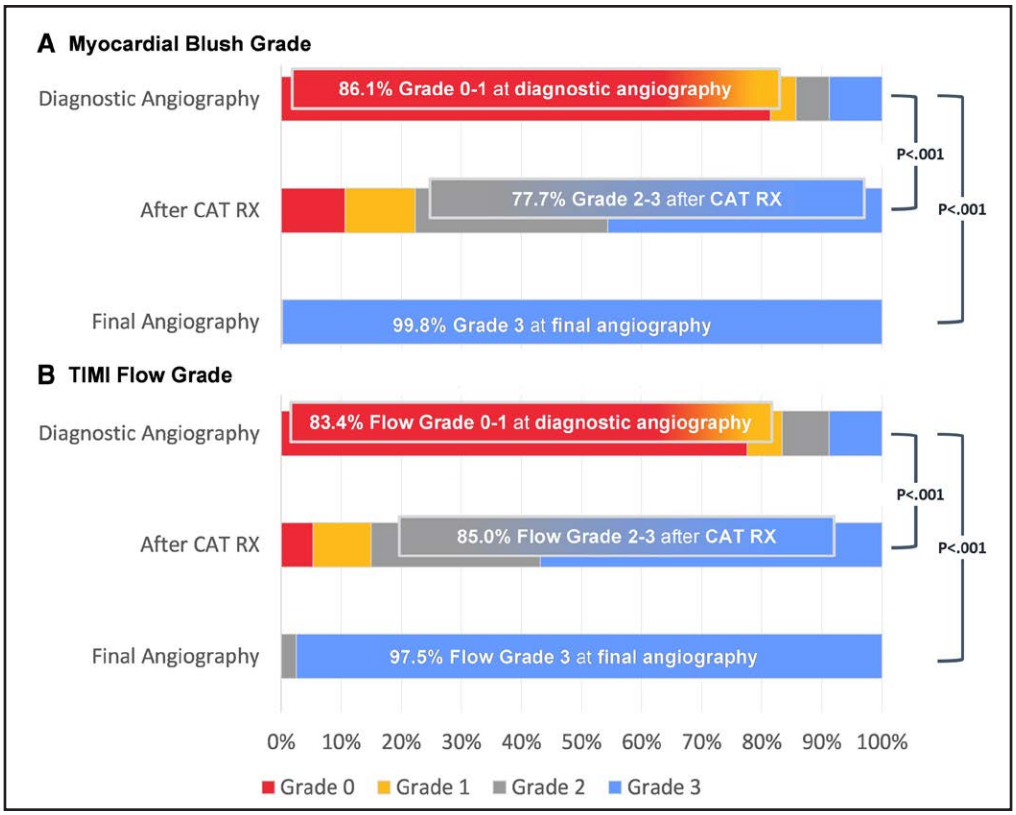

Figure 3. Core laboratory assessment of myocardial blush grade and Thrombolysis in Myocardial Infarction (TIMI) flow grade. Core laboratory assessments of (**A**) myocardial blush grade and (**B**) TIMI flow grades at diagnostic coronary angiographic assessment, after aspiration with CAT RX, and at final coronary angiographic assessment.

expose the limitations of the devices and techniques used previously. During manual aspiration thrombectomy, aspiration force rapidly drops with time,[17] and mechanical thrombectomy employs clot fragmentation and other mechanisms (eg, saline jets) that may push clot distally and increase infarct size. Distal embolization increases microvascular obstruction and is associated with lower MBG.[29]

Stent thrombosis within the CHEETAH study was 2.43%. While direct comparisons cannot be made due to variability in populations, our stent thrombosis rate is in line with the rates previously reported in other ACS trials (2.4–3.9%).[30,31] Additionally, in large studies, the most common independent predictors of definite or probable stent thrombosis are diabetes, ACS at admission, total stent number/length, antiplatelet therapy discontinuation before 30 days, and extent of coronary disease.[30]

Stroke is a known complication of PCI with or without thrombectomy, and carotid disease, cardiogenic shock, atrial fibrillation, and older age are strong predictors.[32] In CHEETAH, stroke occurred in 3 patients. One occurred well after the index procedure, at day 20. A second patient presented with neurologic complaints prior to primary PCI for STEMI, and was evaluated by a stroke neurologist who concluded that the presence of stroke at the time was uncertain. Unfortunately, neurologic complaints continued to evolve with stroke confirmed by magnetic resonance imaging 3 days post-procedure. A third patient had a periprocedural neurologic event with an National Institutes of Health Stroke Scale increase score of <4 at 24 hours after neurologic event onset. This patient required excessive guide catheter manipulation with multiple guiding catheters to select an anomalous right coronary ostium. It is conceivable that this may have contributed to the patient's neurologic event. The stroke rate in TOTAL's thrombus aspiration group was higher periprocedurally as well as beyond the first 30 days; however, there were a relatively small number of events.[12] In the contemporary SCAAR registry (Swedish Coronary Angiography and Angioplasty Registry) of 42 829 patients, no stroke signal was found in patients with aspiration thrombectomy STEMI PCI.[33] The risk of stroke with continuous aspiration thrombectomy needs to be further investigated in a randomized controlled trial.

Other Variables of Interest

The median total aspiration time was 69 seconds. When a manual aspiration syringe is on nonocclusive thrombus or within an open vessel, it is unable to maintain vacuum force as the syringe fills. An in vitro experiment

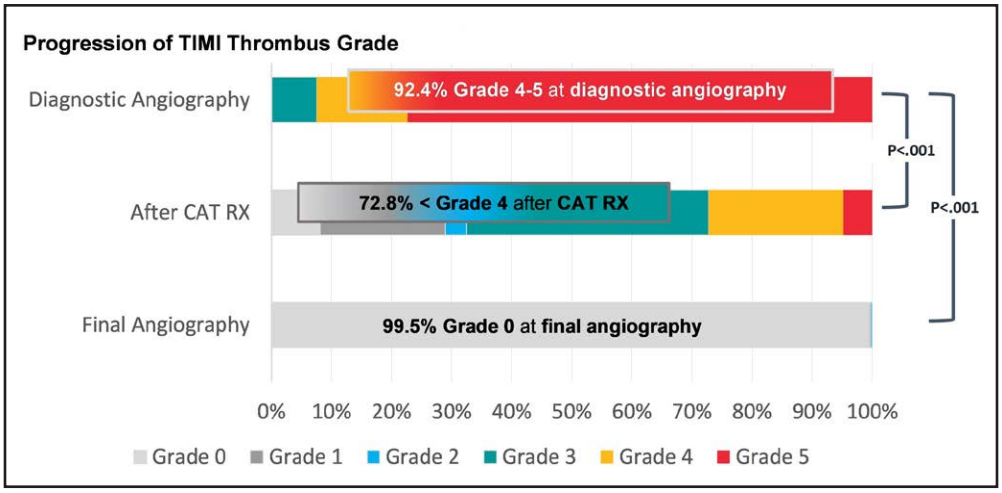

Figure 4. Core laboratory assessment of Thrombolysis in Myocardial Infarction (TIMI) thrombus grade.
Core laboratory assessments of TIMI thrombus grade at diagnostic coronary angiographic assessment, after aspiration with CAT RX, and at final coronary angiographic assessment.

comparing manual VacLok syringe (Merit Medical System Inc, South Jordan, UT) aspiration with the Penumbra Pump MAX found that while the 60 mL syringe initially created higher flow rates than the pump for approximately the first 2 seconds, the flow rate rapidly dropped after ~10 seconds.[17] In contrast, the pump produced relatively constant flow throughout the entire duration of the experiment.[17] The mean door-to-device (59.4 minutes) and door-to-reperfusion (63.9 minutes) times for STEMI patients were well within the current target door-to-device time of ≤90 minutes.[3] These times also compared favorably to the median door-to-device time of 61 minutes described in the National Cardiovascular Data Registry CathPCI registry 2019 to 2020 report.[34] Within the CHEETAH study, the Indigo CAT RX Aspiration System was associated with short procedure times (mean [SD] access-to-reperfusion time was 18.4 [12.5] minutes). Glycoprotein IIb/IIIa inhibitor use in our study was per operator discretion. Its use was numerically lower than the rate reported in the TOTAL study's high thrombus burden population (33.25% versus 40.80%, respectively) and had no impact on that study's results.[12,21] This decreased use may reflect the current pharmacologic management of acute MI. In addition, study operators reported improved visualization of the culprit lesion in 94.72% of cases. With high thrombus burden, a leading column of thrombus or static blood may obscure a more focal underlying lesion. This can result in PCI of uninvolved areas (increasing the risk of intimal injury or dissection and lesion extension) and require longer stents. The CHEETAH study offers compelling evidence that sustained mechanical aspiration thrombectomy in high thrombus burden ACS patients may be beneficial in this regard. Further large, randomized studies will be necessary to validate the encouraging safety and performance results.

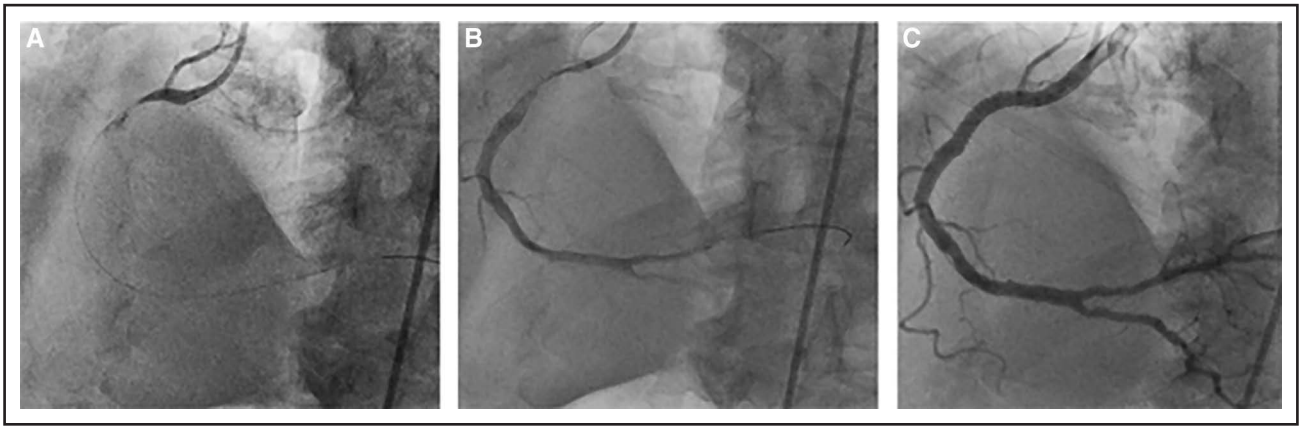

Figure 5. Example case of Indigo CAT RX Aspiration System.
An example of Indigo CAT RX Aspiration System removing thrombus and exposing the underlying focal lesion: (**A**) diagnostic angiogram after wire crossing showing Thrombolysis in Myocardial Infarction (TIMI) flow 0; (**B**) angiogram postthrombectomy with the Indigo CAT RX Aspiration System showing TIMI flow 2; and (**C**) final angiogram showing TIMI flow 3.

Strengths/Limitations

Strengths include prospective, consecutive, multicenter patient recruitment and the use of a centralized core laboratory and independent medical reviewer to assess the outcome measures. Limitations include the lack of randomization, the fact that not all interventional cardiologists at the sites participated in the study. Additionally, the ability to enroll patients up to 2 days postprocedure but prior to discharge may have introduced selection bias. Study enrollment and screening occurred during the COVID-19 pandemic, introducing challenges to obtaining consent prior to procedure as legally authorized representatives may have been restricted from entering the hospital. However, a concerted effort was made to enroll consecutive patients. Screen failures were logged and the most common reasons were inadequate thrombus burden and lack of up front CAT RX use. The reasons for exclusion are not mutually exclusive. Furthermore, while MBG was assessed by a core laboratory, the clinical operators did not capture angiographic images using a prespecified blush protocol;[35] this may have introduced measurement bias. Additionally, the number of patients and operators were relatively small compared to prior large meta-analyses and randomized trials that reported lower rates of MBG 3 with thrombectomy compared to the rates seen in CHEETAH.

Conclusions

The CHEETAH study results suggest that selective sustained mechanical aspiration thrombectomy in high thrombus burden ACS patients prior to PCI may be appropriate. We found that the Indigo CAT RX Aspiration System was safe and associated with reduction of thrombus burden, restoration of flow, and normalization of myocardial perfusion. To further validate the results from CHEETAH and utility of aspiration thrombectomy with CAT RX, a randomized controlled trial is needed and in development.

ARTICLE INFORMATION

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Supplemental Material

Listing S1
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