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Comparison of bolus versus continuous thermodilution derived indices of microvascular dysfunction in revascularized coronary syndromes

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ABSTRACT

Background: The assessment of coronary microvascular dysfunction (CMD) using invasive methods is a field of growing interest, however the preferred method remains debated. Bolus and continuous thermodilution are commonly used methods, but weak agreement has been observed in patients with angina with non-obstructive coronary arteries (ANOCA). This study examined their agreement in revascularized acute coronary syndromes (ACS) and chronic coronary syndromes (CCS) patients.

Objective: To compare bolus thermodilution and continuous thermodilution indices of CMD in revascularized ACS and CCS patients and assess their diagnostic agreement at pre-defined cut-off points.

Methods: Patients from two centers underwent paired bolus and continuous thermodilution assessments after revascularization. CMD indices were compared between the two methods and their agreements at binary cut-off points were assessed.

Results: Ninety-six patients and 116 vessels were included. The mean age was 64 ± 11 years, and 20 (21 %) were female. Overall, weak correlations were observed between the Index of Microcirculatory Resistance (IMR) and continuous thermodilution microvascular resistance (R_{μ}) (rho = 0.30p = 0.001). The median coronary flow reserve (CFR) from continuous thermodilution (CFR_{cont}) and bolus thermodilution (CFR_{bolus}) were 2.19 (1.76–2.67) and 2.55 (1.50–3.58), respectively ($p < 0.001$). Weak correlation and agreement were observed between CFR_{cont} and CFR_{bolus} (rho = 0.37, $p < 0.001$, ICC 0.228 [0.055–0.389]). When assessed at CFR cut-off values of 2.0 and 2.5, the methods disagreed in 41 (35 %) and 45 (39 %) of cases, respectively.

Conclusions: There is a significant difference and weak agreement between bolus and continuous thermodilution-derived indices, which must be considered when diagnosing CMD in ACS and CCS patients.

1. Introduction

The invasive assessment of coronary microvascular dysfunction (CMD) is a rapidly growing space within the field of interventional cardiology, particularly in patients with angina with non-obstructive coronary arteries (ANOCA), where it is has gained widespread traction following the CORMICA (Coronary Microvascular Angina) trial[1]. Subsequently, the invasive assessment of CMD in INOCA has garnered a class IIa recommendation for use in the European Society of Cardiology (ESC) chronic coronary syndromes (CCS) guidelines[2].

CMD, however, is not simply limited to INOCA patients. In CCS patients undergoing percutaneous coronary intervention (PCI), up to one third continue to have ongoing angina despite revascularisation [3], of

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Nomenclature

Abbreviations

ACS	Acute coronary syndromes
CCS	Chronic coronary syndromes
CFR	Coronary flow reserve
CMD	Coronary microvascular dysfunction
EF	Ejection fraction
ESC	European Society of Cardiology
FFR	Fractional flow reserve
IMR	Index of Microcirculatory Resistance
ANOCA	Angina with non-obstructive coronary arteries
IV	Intravenous
LAD	Left Anterior Descending
MRR	Microvascular Resistance Reserve
Pa	Coronary artery pressure
PCI	Percutaneous coronary intervention
RRR	Resistance Reserve Ratio
Rμ	Microcirculatory resistance
STEMI	ST elevation myocardial infarction
WU	Wood units

which CMD is hypothesised to play a substantial role[4]. Additionally, in acute coronary syndromes (ACS), microvascular dysfunction following revascularisation is present in up to 50 % of patients, despite timely reperfusion [5]. Furthermore, in ST elevation myocardial infarction (STEMI), microvascular dysfunction is associated with adverse clinical outcomes including all-cause mortality, hospitalization with heart failure within 1 year and early major cardiac complications[6–8].

Despite this widespread clinical applicability, the optimal methodology of invasively diagnosing and quantifying CMD remains debatable [9]. Contributing to this debate is the variety of methods and technologies used to diagnose CMD. Specifically, over the last three decades, the technology has evolved from early Doppler guidewires [10] to bolus thermodilution [11]and more recently continuous thermodilution [12]. Doppler is considered by many as representing the invasive reference standard measurement [13], however, the current technology is hampered by technical difficulties, particularly the difficulty in achieving adequate Doppler envelopes in up to a third of cases[14] and the lack of availability of Doppler wires and consoles. As a result, bolus thermodilution is currently the most widely utilised method for invasive CMD assessment, however it is not without its own pitfalls. Recently, bolus thermodilution has been shown to systematically overestimate Coronary Flow Reserve (CFR) relative to Doppler[13] and has previously been shown to have less correlation with (^{15}O)$H_2$0PET[15]. Finally, continuous thermodilution is now under the spotlight as it has so far been shown to be safe, easy to perform and more reproducible than bolus thermodilution [17–19]. However more data and validation are required before it can gain widespread adoption in the clinical practice.

For this reason, the aim of this study is to compare bolus thermodilution and continuous thermodilution derived indices of CMD in revascularized ACS and CCS patients, and to assess their agreements as diagnostic tools at pre-defined cut-off points.

2. Methods

2.1. Study design and population

This is a collaborative study involving two centres conducting independent observational cohort studies. The Essex Stable Angina and Acute Myocardial Infarction (Essex-SAAMI) study (*REC reference 22/EE/0016*), and the Oxford Acute Myocardial Infarction (OxAMI) study (REC Reference: 11/SC0397) are prospective, observational studies, investigating coronary physiology in both culprit and non-culprit vessels in chronic coronary syndrome (CCS) and acute coronary syndromes (ACS) including both STEMI and non-STEMI patients. Inclusion and exclusion criteria for both studies are provided in the supplemental methods. In culprit vessels, for the purpose of the current study, invasive physiological assessment was performed at the end of the percutaneous coronary intervention (PCI). All patients provided written informed consent and the studies had local regional ethical committee approval. The STEMI patients in both Essex-SAAMI and OxAMI provided initial verbal consent before later providing written consent in line with study protocols. The studies adhered to the principles of the declaration of Helsinki.

2.2. Percutaneous coronary intervention

Coronary angiography was performed via the radial or femoral arteries using 6Fr catheters. Percutaneous coronary intervention was performed according to operator preference using a wide array of adjuncts and intracoronary imaging modalities in line with contemporary standards. There were no pre-mandated requirements for intracoronary imaging, stent platform, or the type of angioplasty performed (stent, drug-coated balloon, or balloon only).

2.3. Physiological measurements

Physiological measurements were performed using a combined pressure/thermistor guidewire (Pressure Wire X™, Abbott Vascular, St Paul, MN), a dedicated monorail infusion microcatheter (Rayflow, Hexacath Paris, France) and a proprietry software system (Coroventis CoroFlow v3.01, Uppsala, Sweden). Hyperemic conditions for bolus thermodilution were induced using a peripheral intravenous (IV) infusion of adenosine at a dose of 140mcg/kg/min according to local protocols. Intracoronary nitrates (Isosorbide Dinitrate) were given in all cases in varying amounts (minimum of 200mcg). Bolus thermodilution measurements were performed first, with continuous thermodilution measurements performed second after allowing the adenosine-induced hyperemic conditions to subside.

2.4. Coronary flow reserve calculation

The bolus thermodilution method was used to derive resting mean transit time (Tmn_{rest}) and hyperemic mean transit time (Tmn_{hyper}) in seconds (s) as described in previous literature ([16]). The Coroflow software was used to calculate a CFR from bolus thermodilution (CFR_{bolus}), defined as the ratio of $1/Tmn_{hyper}$ to $1/Tmn_{rest}$: $CFR_{bolus}=(1/Tmn_{hyper})/(1/Tmn_{rest})$ which can further be simplified as:

$$CFR_{Bolus} = \frac{Tmn_{rest}}{Tmn_{hyp}}$$

The continuous thermodilution method was performed according to previously described methodology[17]. Both centres performed a continuous recording of low flow (8–10 ml/min) and high flow (15–20 ml/min) infusions of room temperature saline to derive a resting (Q_{rest}) and hyperemic (Q_{hyp}) absolute coronary blood flow (ABF) respectively. The continuous thermodilution derived CFR (CFR_{cont}) was calculated as the ratio of Q_{hyp} and Q_{rest}.

$$CFR_{Cont} = \frac{Q_{hyp}}{Q_{rest}}$$

2.5. Microvascular Resistance Reserve, Resistance Reserve Ratio, and Index of Microcirculatory Resistance Calculation, hyperemic microvascular Resistance

Microvascular Resistance Reserve (MRR) was derived using the continuous thermodilution method as described earlier. MRR, defined as

the ratio of true resting resistance to hyperemic resistance corrected for driving pressures, was calculated using the equation below as described in previous literature[18]:

$$MRR = \frac{CFR}{FFR} \times \frac{Pa_{rest}}{Pa_{hyp}}$$

The Index of Microcirculatory Resistance (IMR) was derived using bolus thermodilution. The equation as previously described in the literature was [19]:

$$IMR = Tmn_{hyp} \times Pd_{hyp}$$

Resistance Reserve Ratio (RRR) was derived using bolus thermodilution method as described earlier. RRR is defined as the ratio of hyperemic resistance to resting resistance using the equation below[20]:

$$RRR = \frac{Tmn_{rest} \times Pd_{rest}}{IMR}$$

Hyperemic Microvascular Resistance (R_μ) was derived using continuous thermodilution as described in previous literature[21]. The equation for R_μ is:

$$R_\mu = \frac{P_d}{Q}$$

2.6. Statistical analysis

Continuous data are expressed as mean (±standard deviation) or median (25th and 75th percentile) depending on the distribution of data. Categorical data are expressed as percentages. Normality of data distribution was first assessed by the Shapiro-Wilk test. Comparisons of data were performed using Paired T-test, Wilcoxon signed rank test, or Kruskal-Wallis / one-way ANOVA, as appropriate. Correlations were assessed using Pearson's r, or Spearman's rho, as appropriate. Agreements were assessed using Bland-Altman plots, and Intra-class Correlation coefficient calculated using a two-way mixed-effect model with measures of absolute agreement. Agreement at binary cut-off points was assessed using Cohen's Kappa at the cut-off points of 2.0 and 2.5. Statistical analysis was performed using SPSS Statistics (IBM, New York, United States).

3. Results

3.1. Study population

A total of 96 patients underwent physiological assessment across 2 cohorts (CCS 37, ACS 59). The mean age was 64 ± 11 and 20 (21 %) were female. The mean left ventricular EF% was 52 ± 7. A history of diabetes mellitus was present in 18 (19 %) patients. Full patient characteristics are displayed in Table 1. A total of 116 vessels were interrogated (47 in CCS, 69 ACS), of which 35 (30 %) were reference vessels (Table 1). The left anterior descending (LAD) was the interrogated vessel in 62 (53 %) physiological assessments (Table 1).

3.2. Physiological measurements

A summary of physiological measurements from bolus and continuous thermodilution with associated p values can be viewed in Table 2. A further breakdown of physiological measurements by cohort can be seen in the supplementary materials **(Supplementary Table 1)**.

3.3. Resting and hyperemic pressure ratios

Overall, there was a significant difference between resting P_d/P_a values recorded during bolus and continuous thermodilution methods (0.97 ± 0.05 and 0.94 ± 0.05 respectively, mean difference = 0.02, p < 0.001) **(Supplementary Table 2)**. Similarly, there was a significant difference between FFR values (bolus thermodilution FFR = 0.91 ± 0.08, continuous thermodilution FFR = 0.86 ± 0.08), mean difference 0.05, p < 0.001). A similar trend was noted when assessed by cohort, and by target / reference vessels individually **(Supplementary Table 2)**.

Table 1
Patient and Vessel Characteristics for all patients, CCS patients, and ACS patients. CCS: Chronic Coronary Syndrome, ACS: Acute Coronary Syndrome.

	Mean +/- SD *or* N (%)		
	All	**CCS**	**ACS**
Patients	96	37 (39 %)	59 (61 %)
Cumulative Vessels	116	47 (41 %)	69 (59 %)
LAD	62 (53 %)	23 (49 %)	39 (57 %)
Reference Vessels	35 (30 %)	23 (26 %)	12 (17 %)
Age	64 ± 11	64 ± 11	64 ± 11
Female	20 (21 %)	7 (19 %)	13 (22 %)
Family history CAD	36 (38 %)	15 (41 %)	21 (36 %)
Hypertension	57 (59 %)	23 (62 %)	34 (58 %)
Diabetes Mellitus	18 (19 %)	4 (11 %)	14 (24 %)
Hypercholesterolaemia	39 (41 %)	15 (41 %)	24 (41 %)
Left Ventricular EF%	52 ± 7	54 ± 6	51 ± 8
Previous Myocardial Infarction	24 (25 %)	15 (41 %)	9 (41 %)
Previous CABG	1 (1 %)	1 (3 %)	0 (0 %)
Previous PCI	26 (27 %)	18 (49 %)	8 (14 %)
Smoking history	50 (52 %)	17 (46 %)	33 (56 %)
Chronic Kidney Disease	5 (5 %)	3 (8 %)	2 (3 %)
Peripheral Vascular Disease	3 (3 %)	2 (5 %)	1 (2 %)
Previous CVA/TIA	3 (3 %)	1 (3 %)	2 (3 %)

Table 2
Physiological measurements of bolus thermodilution and continuous thermodilution.

	Continuous Thermodilution	**Bolus Thermodilution**	**P value**
CFR	2.19 (1.76–2.67)	2.55 (1.50–3.58)	p < 0.001
MRR	2.67 (2.17–3.37)	–	–
Q_{rest} (ml/min)	75 (54–97)	–	–
Q_{hyp} (ml/min)	170 (118–225)	–	–
$R_{\mu,\ rest}$ (WU)	1253 (918–1591)	–	–
$R_{\mu,\ hyp}$ (WU)	461 (354–666)	–	–
Tmn_{rest} (s)	–	0.80 (0.52–1.12)	–
Tmn_{hyp} (s)	–	0.29 (0.19–0.50)	–
IMR	–	21 (14–35)	–
RRR	–	3.20 (2.00–5.15)	–

3.4. Coronary flow and microcirculatory resistance assessed by bolus and continuous thermodilution

Overall, absolute flow at rest (Q_{rest}) and hyperemia (Q_{hyp}) assessed by continuous thermodilution were 75 (54–97) ml/min and 170 (118–225) ml/min (Table 2.0), respectively, with no significant difference in Q_{rest} values between cohorts (p = 0.296), and Q_{hyp} values between cohorts (p = 0.195) **(Supplementary Table 3)**. Microcirculatory

resistance at rest ($R_{\mu, rest}$) and hyperemia ($R_{\mu, hyp}$) across all cohorts were 1253 (918–1591) WU and 461 (354–666) WU, respectively. Similarly, there were no significant differences in R_{μ} values between cohorts **(Supplementary Table 3).**

There was no significant difference between Tmn_{rest} values between cohorts (p = 0.965), however a significant difference between Tmn_{hyp} values was noted between cohorts (p = 0.004) **(Supplementary Table 3).** Accordingly, a significant inter-cohort difference in IMR values was also seen (p = 0.004) **(Supplementary Table 3).**

A weak correlation was noted between Tmn_{rest} and Q_{rest} (rho = 0.24, p = 0.009), and Tmn_{hyp} and Q_{hyp} (rho = 0.31, p < 0.001) **(Supplementary figure 1).** A similar trend was noted across all cohorts, with either weak or absent correlations between bolus and continuous thermodilution derived flow indices **(Supplementary figure 2).** Similarly, a weak correlation was observed between $R_{\mu, hyp}$ and IMR overall (rho = 0.30, p < 0.001) (Fig. 1), with further weak or absent correlations assessed by cohort, apart from CCS where a moderate correlation was seen (rho = 0.60, p = 0.002) **(Supplementary figure 3).**

3.5. Comparison between bolus and continuous thermodilution derived coronary flow reserve and resistance reserve indices (MRR, RRR)

The median CFR_{cont} and CFR_{bolus} were 2.19 (1.76–2.67) and 2.55 (1.50–3.58), respectively (p < 0.001). Only a weak correlation was found between CFR_{cont} and CFR_{bolus} (rho = 0.37p < 0.001), with Bland-Altman analysis showing a significant mean bias of 0.68 (p < 0.001) and weak agreement (ICC 0.228 [0.055–0.389]) (Fig. 2). Similar trends were noted across ACS, CCS, and reference vessels individually **(Supplementary figure 4),** although there was no significant difference between CFR_{bolus} and CFR_{cont} values in the ACS cohort.

A moderate correlation was found between MRR and RRR (rho = 0.44, p < 0.001) (Fig. 2).

As binary diagnostic tools assessed at CFR cut-off values of 2.0 and 2.5, bolus and continuous thermodilution derived CFR disagreed in 41 (35 %) and 45 (39 %) of cases respectively (Cohen's Kappa 0.249 and 0.247 respectively) **(**Fig. 3**).**

4. Discussion

4.1. Summary of results

The present study is the first to direct compare bolus versus continuous thermodilution derived flow and flow-derived indices in both CCS and ACS patients undergoing PCI. The key findings of this study are as follows. Firstly, there existed only weak or no correlations between Tmn and Q that underpin the synthesis of subsequent indices of CMD. Secondly, the CFR values determined by bolus and continuous thermodilution demonstrated weak agreement, particularly when applied as binary classification tools. Lastly, in line with previous literature, a significant difference in FFR values achieved between the methodologies was noted.

4.2. Comparison of mean transit time (Tmn) and absolute flow (Q)

Our results identified only weak or no correlation between bolus thermodilution derived 1/Tmn, and continuous thermodilution derived Q across both reference and target vessels (at rest and hyperemia). Notably, the correlations were significantly worse for the resting flow measurements (Tmn_{rest} and Q_{rest}). This may be due to high variability in resting conditions. Ultimately, it is the weak, or lack of, correlations between these flow metrics that results in significant disagreement between the subsequent bolus and continuous thermodilution derived indices used in clinical decision-making. Of note, no significant differences of continuous thermodilution derived Q (and therefore R_{μ}) between cohorts was observed however this can be explained by the heterogenicity of absolute flow measurements across differing vessels (Supplementary Table 4) and myocardial territories subtended.

4.3. Comparison of bolus and continuous thermodilution derived indices

With regards to CFR, the present study demonstrated a significant difference between CFR values obtained from bolus and continuous thermodilution indices. Notably, Bland-Altman plots demonstrated a significant positive bias between CFR values derived from bolus versus continuous thermodilution. Additionally, the relationship was heteroscedastic, driven by seemingly supraphysiological results obtained by

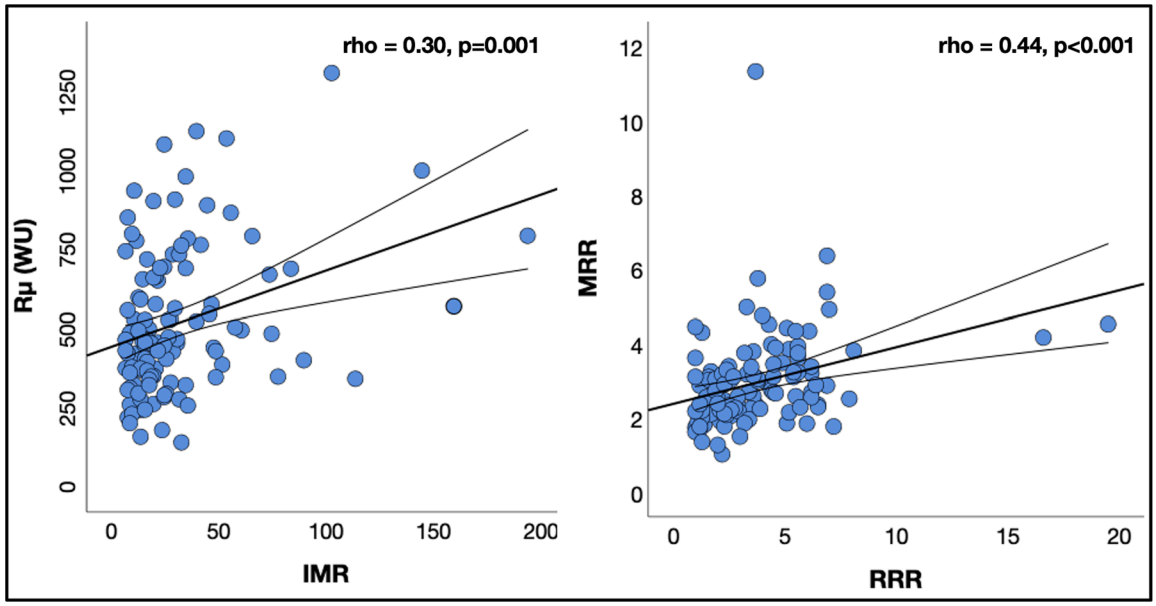

Fig. 1. Scatter plots of Continuous versus Bolus Thermodilution microvascular indices. Scatter plots of (Left) Rμ against IMR, and (right) MRR against RRR. (Rμ = Hyperemic Microvascular Resistance, WU = Wood's Units, IMR = Index of Microcirculatory Resistance, MRR = Microvascular Resistance Reserve, RRR = Resistance Reserve Ratio, rho = Spearman's rho correlation).

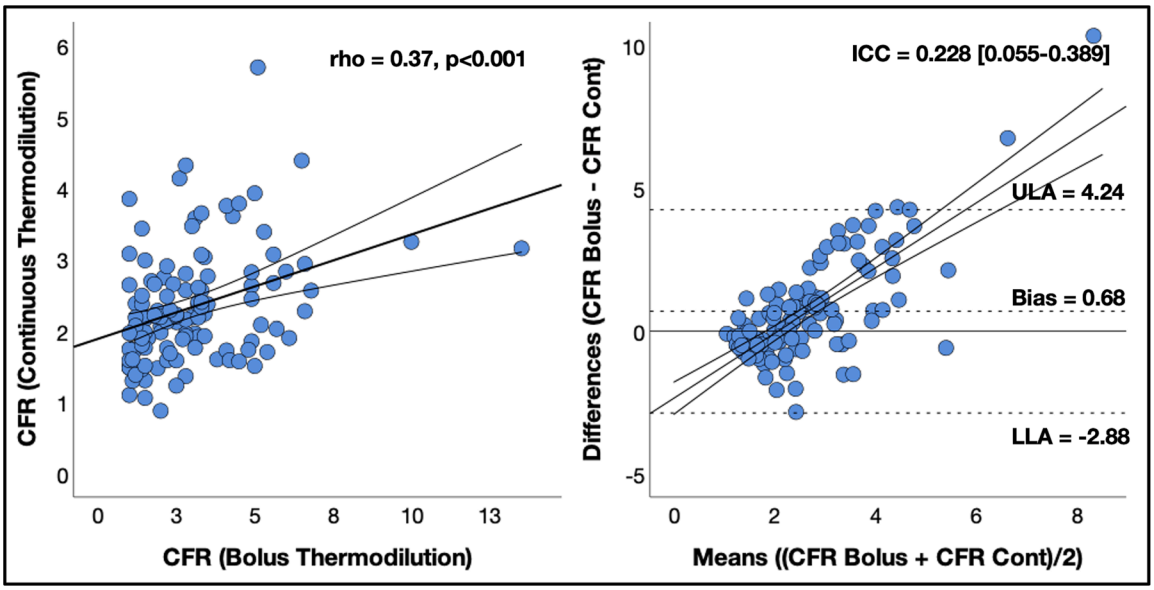

Fig. 2. Scatter plot and Bland-Altman plot of CFR_{cont} versus CFR_{bolus}. Scatter plot (left) of CFR_{cont} (y-axis) and CFR_{bolus} (x-axis) with corresponding Bland-Altman plot (right). (CFR = Coronary flow reserve, CFR_{cont} = Continuous thermodilution CFR, CFR_{bolus} = Bolus Thermodilution CFR, ULA = Upper limit of agreement, LLA = Lower limit of agreement), rho = Spearman's rho correlation, ICC = intra-class correlation coefficient.

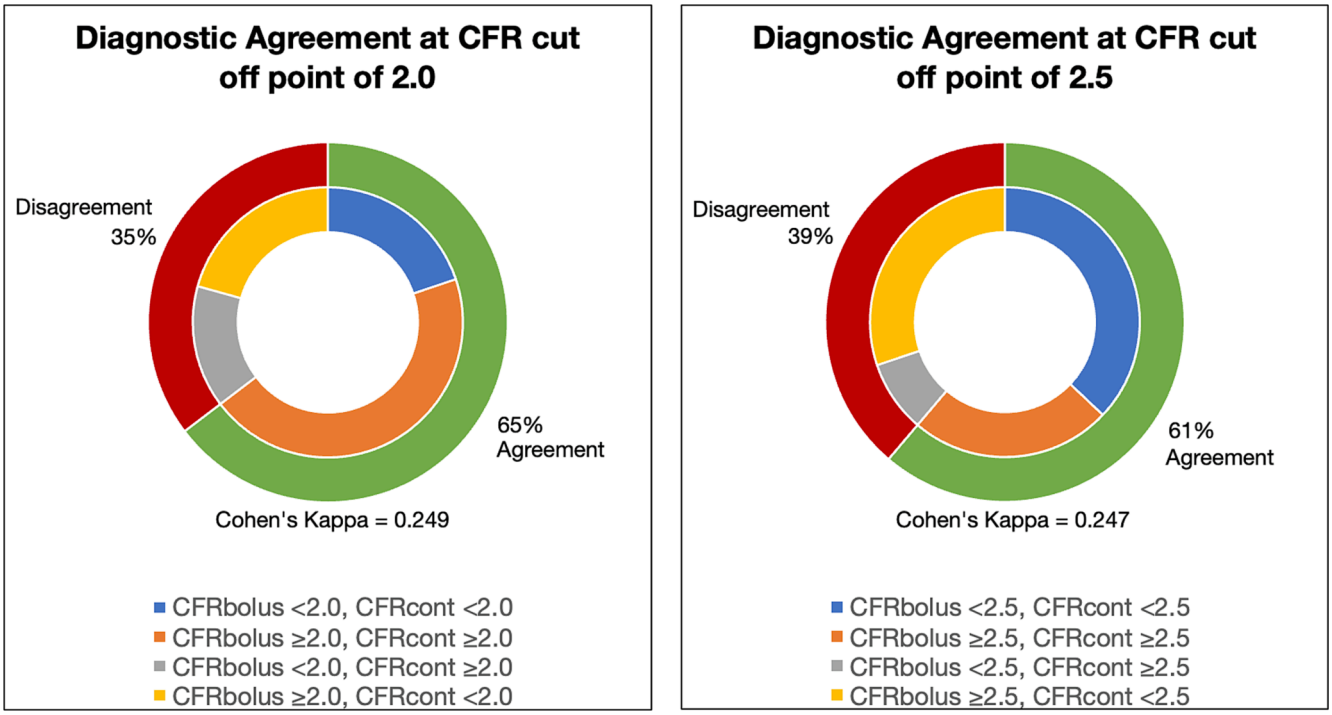

Fig. 3. Diagnostic Agreement of CFR_{cont} and CFR_{bolus}. Pie charts of the Diagnostic Agreement of CFR_{cont} and CFR_{bolus} at cut-off points 2.0 (left) and 2.5 (right) with associated Cohen's Kappa statistic. (CFR_{cont} = Continuous thermodilution derived Coronary Flow Reserve, CFR_{bolus} = Bolus thermodilution derived Coronary Flow Reserve).

the CFR_{bolus} method; a consistent finding in the literature [13,22]. Furthermore, the intra-class correlation coefficient across ACS, CCS, and reference vessels expressed only a weak agreement between bolus and continuous thermodilution methodologies, resulting in frequent misclassification when used as binary diagnostic tools at both CFR < 2.0 and CFR < 2.5 cut-off values. This finding is in contrast with an earlier study in INOCA patients that showed a good correlation and agreement between the methodology[17]. Conversely, the present study findings are consistent with more recent literature where similarly only a weak correlation and agreement between bolus and continuous thermodilution derived indices were demonstrated[22]. Our study demonstrates a similar finding when analysed according to MRR and RRR indices also.

Therefore, there appears to be multiple considerations in the use of bolus thermodilution to reliably diagnose and quantify CMD. Specifically, in recent literature, bolus thermodilution has been shown to have only a modest correlation with the widely accepted invasive gold standard of intracoronary Doppler, and to systematically overestimate CFR relative to Doppler as well [13]. Moreover, it displays more inter and

intra-observer variability versus Doppler and less correlation with non-invasive (^{15}O)$H_2$0PET imaging [23]. Additionally, compared to continuous thermodilution, bolus thermodilution has been shown to have more variability and inferior reproducibility[22]. A possible explanation for this observation is that the inverse of mean transit time (a surrogate for actual coronary flow), is affected by the quality and consistency of injections, guide position (and damping), and sensor wire position[14]. In contrast, continuous thermodilution seems to present a robust, reproducible, and less operator-dependent method of deriving CFR[17], with good correlation with Doppler CFR[18], and non-invasive (^{15}O)$H_2$0PET[15] methods. Furthermore, the continuous thermodilution method does not require the administration of pharmacological vasodilators (hyperemic agents), as is the case in bolus thermodilution, thereby reducing the impact on overall haemodynamic status, and therefore coronary flow, whilst reducing the incidence of side effects and increasing the availability of testing to those with contraindications to commonly used agents such as adenosine.

However, continuous thermodilution is not without procedural limitations or considerations. Specifically, the proprietary Rayflow catheter is likely to induce a progressively significant obstruction to flow in more stenotic epicardial vessels, and thus introduce a bias to CFR, FFR, Pd and resistance measurements [22]. This potential source of bias may be accounted for by MRR measurement, which is considered independent of epicardial stenosis severity [18]. Moreover, in addition to the equipment required for bolus thermodilution, continuous thermodilution requires a dedicated infusion microcatheter and an infusion pump programmable in mL/min, therefore increasing overall cost. Additionally, and most importantly, there currently exists no clinical outcome data for continuous thermodilution derived indices. However, clinical studies assessing this (European Microcirculatory Group *(EuroCRAFT study NCT04598308)* are currently recruiting. In contrast, the established bolus thermodilution method, and the resultant indices, do have clinical outcome data to support their clinical use [9], especially in the STEMI field where bolus thermodilution offers a good compromise between diagnostic accuracy and ease of use that is pivotal in the emergency setting [24]. Lastly, we did not observe an inter-cohort difference in CFR values obtained by continuous thermodilution despite noting an inter-cohort difference in those obtained by bolus thermodilution. The lack of a third comparator renders this finding difficult to rationalise.

Of interest, in the contemporary study by de Vos et al, a normal and abnormal range for MRR has been suggested, with a subsequent "grey zone" in between [25]. Accordingly, "grey zones" may prove more helpful in the diagnostic process of CMD as opposed to the application of binary cut-offs for clinical decision-making. Furthermore, a notable study by Jansen et al. demonstrated no correlation between angina scoring questionnaires for both bolus and continuous thermodilution derived CFR and MRR, however a significant correlation for only continuous thermodilution derived CFR and MRR in physical health components of the questionnaires [26].

4.4. Discrepancy in FFR values

In accordance with prior reports, in the present study we also demonstrated a significant difference between FFR values obtained by bolus versus continuous thermodilution methods. This mean difference of ~ 0.03 FFR units has previously been explained by the direct haemodynamic impact of the Rayflow catheter[21]. However, in our study, we noted a numerically higher FFR mean difference (0.05 FFR units). Of note, although the FFR from continuous thermodilution is lower relative to that of bolus thermodilution, this did not correspond with a higher CFR overall when compared to bolus thermodilution.

5. Limitations

The present study is not without limitations. First, bolus thermodilution measurements were performed by multiple operators. Accordingly, our results may be influenced by heterogeneity in measurement technique. This, however, is illustrative of real-world clinical scenarios. Second, there is no third comparator in this study, although bolus and continuous thermodilution have previously been compared to Doppler[13,18], and (^{15}O)$H_2$0PET[15] individually. Ideally, a dedicated head-to-head comparison is needed. Third, although this is the largest known study of paired continuous and bolus thermodilution derived physiology in ACS and CCS patients undergoing PCI, the sample size is still modest. Fourth, continuous thermodilution measurements were performed after bolus thermodilution measurements, and although both sites allowed ample time for the effects of adenosine to wear off, no pre-specified time was stated in the protocols. Consequently, it is impossible to fully exclude the effect of residual hyperemia on continuous thermodilution measurements. Finally, no difference was noted between CFR_{bolus} and CFR_{cont} values in the ACS cohort, however, a post-hoc power calculation has shown insufficient power to detect this change. Accordingly, the weak agreement demonstrated by ICC and Bland-Altman must be considered when addressing this finding.

6. Conclsusions

Overall, our study demonstrates the clinical feasibility of performing CMD assessments using continuous and bolus thermodilution in both ACS and CCS patients undergoing percutaneous coronary intervention. However, there exists a significant difference and weak agreement between the resultant indices that must be considered when used to diagnose CMD.

Disclosures.

Christopher M Cook is a consultant for Philips Healthcare and Viz.ai, receives speaker fees from Boston Scientific and has equity in Cerebria.ai. John R Davies has received research grants from Abbott Vascular and Medtronic, and has received speaker fees from Boston Scientific. Giovanni L De Maria has received research grants from Medtronic, Philips, Terumo and Opsens. Thomas R Keeble has received honoraria and institutional research funding from Abbott Vascular, Medtronic, Hexacath, Terumo, Zoll and Shockwave; consulting fees from BD; and speaker fees from Cardionovum, Abbott Vascular and Astra Zeneca. Thomas R Keeble is on the steering group for the ORBITA-2 trial and on the committee for National Institute for Health and Care Research Invention for Innovation (i4i), British Cardiovascular Intervention Society and Resuscitation Council (UK). Grigoris V Karamasis has received support from Abbott Vascular. The other authors have no disclosures.

CRediT authorship contribution statement

Samer Fawaz: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Federico Marin:** Conceptualization, Data curation, Investigation, Methodology, Writing – review & editing. **Sarosh A Khan:** Formal analysis, Investigation, Writing – review & editing. **Rupert F G Simpson:** Data curation, Investigation, Methodology, Writing – review & editing. **Rafail A Kotronias:** Data curation, Investigation, Writing – review & editing. **Jason Chai:** Data curation, Investigation, Writing – review & editing. **Oxford Acute Myocardial Infarction OxAMI Study Investigators:** . **Firas Al-Janabi:** Investigation, Writing – review & editing. **Rohan Jagathesan:** Data curation, Investigation, Writing – review & editing. **Klio Konstantinou:** Data curation, Investigation, Writing – review & editing. **Shah R Mohdnazri:** Data curation, Investigation, Writing – review & editing. **Gerald J Clesham:** Data curation, Investigation, Writing – review & editing. **Kare H Tang:** Data curation, Investigation, Writing – review & editing. **Christopher M Cook:** Conceptualization, Data curation, Investigation, Methodology, Supervision, Writing – review & editing. **Keith M Channon:** Data curation, Investigation, Supervision, Writing – review & editing. **Adrian P Banning:** Data curation, Investigation, Supervision, Writing – review &

editing. **John R Davies:** Conceptualization, Data curation, Investigation, Methodology, Supervision, Writing – review & editing. **Grigoris V Karamasis:** Conceptualization, Formal analysis, Supervision, Writing – review & editing. **Giovanni L De Maria:** Conceptualization, Data curation, Formal analysis, Methodology, Supervision, Writing – review & editing. **Thomas R Keeble:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Supervision, Writing – review & editing.

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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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2024.101374.

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