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ORIGINAL ARTICLE

# Protocol Variation in Functional Coronary Angiography Among Patients With Suspected Angina With Non-Obstructive Coronary Arteries: A Nationwide Snapshot of Current Practice Within Australia and New Zealand

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**Background** Functional coronary angiography (FCA) for endotype characterisation (vasospastic angina [VSA], coronary microvascular disease [CMD], or mixed) is recommended among patients with angina with non-obstructive coronary arteries. Whilst clear diagnostic criteria for VSA and CMD exist, there is no standardised FCA protocol. Variations in testing protocol may limit the widespread uptake of testing, generalisability of results, and expansion of collaborative research. At present, there are no data describing protocol variation across an entire geographic region. Therefore, we aimed to capture current practice variations in the approach to FCA to improve access and standardisation for diagnosis of coronary vasomotor disorders in Australia and New Zealand.

**Method** Between July 2022 and July 2023, we conducted a national survey across all centres in Australia and New Zealand with an active FCA program. The survey captured attitudes towards FCA and protocols used for diagnosis of coronary vasomotor disorders at 33 hospitals across Australia and New Zealand.

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**Results** Survey responses were received from 39 clinicians from 33 centres, with representation from centres within all Australian states and territories and both North and South Islands of New Zealand. A total of 21 centres were identified as having an active FCA program. In general, respondents agreed that comprehensive physiology testing helped inform clinical management. Barriers to program expansion included cost, additional catheter laboratory time, and the absence of an agreed-upon national protocol. Across the clinical sites, there were significant variations in testing protocol, including the technique used (Doppler vs thermodilution), order of testing (hyperaemia resistance indices first vs vasomotor function testing first), rate and dose of acetylcholine administration, routine use of temporary pacing wire, and routine single vs multivessel testing. Overall, testing was performed relatively infrequently, with very little follow-on FCA performed, despite nearly all respondents believing this would be clinically useful.

**Conclusions** This survey demonstrates, for the first time, variations in FCA protocol among testing centres across two entire countries. Furthermore, whilst FCA was deemed clinically important, testing was performed relatively infrequently with little or no follow-on testing. Development and adoption of a standardised national FCA protocol may help improve patient access to testing and facilitate further collaborative research within Australia and New Zealand.

**Keywords** ANOCA • Functional coronary angiography • Microvascular angina • Vasospastic angina • Acetylcholine

# Introduction

Angina with non-obstructive coronary arteries (ANOCA) remains a common clinical finding among patients undergoing invasive coronary angiography for the investigation of suspected ischaemic syndromes [1–4]. ANOCA may result from coronary microvascular disease or vasospasm (microvascular or epicardial spasm), which may be diagnosed using comprehensive physiology testing such as invasive functional coronary angiography (FCA) [5].

Current guidelines (European Society of Cardiology [6], American College of Cardiology/American Heart Association [7], and Japanese Circulation Society [8]) recommend the application of FCA in routine clinical practice among patients with signs and/or symptoms of myocardial ischaemia in the absence of obstructive coronary artery disease, given the demonstrated improvement in cardiovascular outcome, quality of life, and health care cost savings associated with endotype identification and stratified medical therapy [9–12].

However, whilst expert consensus exists about the criteria needed to diagnose ANOCA [13], wide variation exists within testing protocols, which most probably reflects individual clinician training and experience, centre familiarisation, and access to equipment required for testing [14]. The influence of protocol variation on test results and subsequent clinical management remains poorly understood.

Currently there are no national or international data detailing protocol variation in routinely performed FCA. In preparing a binational position statement on FCA, the Cardiac Society of Australia and New Zealand (CSANZ) Coronary Vasomotor Dysfunction Working Group pursued an understanding of current practices within these countries and thus commissioned a comprehensive survey. Accordingly, the objective of this survey was to establish a nationwide perspective on attitudes and procedural practices in FCA across Australia and New Zealand sites, thereby providing insights into institutional protocol variations.

# Methods

## The Survey Cohort Setting

The survey cohort included members of the CSANZ Coronary Vasomotor Dysfunction Working Group and additional individuals from centres that were known to be actively performing coronary physiology assessments.

The CSANZ Coronary Vasomotor Dysfunction Working Group was established in 2021 to facilitate clinical and research activities in coronary vasomotor disorders within Australia and New Zealand. The group members included physicians and researchers with significant experience in the field. With an initial objective to develop a position paper on FCA, the group conducted quarterly and out-of-session meetings to obtain a consensus on the procedure. Hence, the study cohort was an enthusiastic, well-informed, collaborative group that included experienced centres undertaking FCA in Australia and New Zealand.

## The Survey

To establish a snapshot of current practice across testing centres within Australia and New Zealand, a Google Forms–based survey was designed (Appendix 1 - survey). The survey covered the following domains: (1) respondent characteristics (age, gender, occupation, time in practice, whether they worked predominantly in the public or private sector); (2) pre-testing instructions (e.g., cessation of regularly used vasoactive medications); (3) testing technique, including access site preference, order of testing (acetylcholine [ACh] or adenosine-based testing first), pressure–temperature sensor guidewire–based thermodilution vs Doppler wire technique, left vs right coronary artery

testing, and routine use of pre-medication/radial cocktail/temporary pacing wire (TPW); (4) perceived barriers to testing, and (5) future research areas and ideas. Upon discussion with the chair of the Royal Perth Hospital Human Research Ethics Committee, it was deemed that formal ethics approval was not required for the survey, since it represented an observational snapshot of contemporary clinical practice.

## Centre Selection

Between July 2022 and July 2023, an electronic link to the survey was sent to the following: (1) members of the Working Group, (2) centres known to have an active FCA program, or (3) centres known to have equipment for assessing coronary blood flow (ComboWire and ComboMap, Philips Volcano Corporation, San Diego, CA, USA; and/or PressureWire X, Abbott Vascular, Santa Clara, CA, USA and CoroFlow Cardiovascular System, Coroventis Research AB, Uppsala, Sweden). Centres were confirmed to have an active FCA program if respondents confirmed that their centre was performing both (1) measurement of hyperaemia resistance indices (index of microcirculatory resistance [IMR]/index of hyperaemic microvascular resistance [hMR]) and (2) vasospasm testing (with approved institutional access to ACh).

Survey results from all respondents were analysed with regard to respondent characteristics, attitudes towards invasive coronary physiology, and barriers to expanding physiology programs. Responses relating to procedure (FCA)-specific variables were only taken from centres identified to have an active FCA program, and for which procedure-specific information was available so that a per-centre analysis of FCA protocol variation could be performed.

# Results

Between July 2022 and July 2023, 46 individuals from 37 centres in Australia and New Zealand were invited to participate in the survey. Of these, 39 individuals from 33 centres responded (Figure 1 and Table 1), yielding an overall response rate of 89% from clinical centres. Responses were received from representative centres within all Australian states and territories and both North and South Islands of New Zealand (Figure 2). Some centres provided several responses, and given that responses were consistent among respondents from the same centre, these responses were combined to allow a per-centre analysis to be performed for the 33 responding centres.

## Survey Respondent Characteristics

Most respondents were male (85%), with 29 (74%) being interventional cardiologists, seven (18%) non-interventional cardiologists, two cardiology advanced trainees, and one research fellow. Most respondents were early-career professionals (1–10 years; 25/39, 64%), with others being mid-(11–15 years; 5/39, 13%) or senior-career (>15 years; 9/39, 23%) professionals. Twenty (20 [51%]) respondents worked principally in a public institution, with 17 (44%) working in both public and private sectors, and only two physicians (5%) working exclusively in a private institution.

When participants were asked whether results of invasive physiology testing (including coronary flow reserve [CFR] and IMR/hMR) were helpful for patient management, nearly all agreed or strongly agreed that CFR and IMR/hMR were useful when managing their patients (85% and 87%, respectively).

### FCA activity within Australia and New Zealand

From the 33 responding centres, 21 were identified as having an active FCA program. One centre was removed from the analysis, as the respondent from that centre did not perform procedures and was therefore unable to provide procedure-specific information. Another respondent reported performing FCA using the same protocol at two separate institutions; therefore, for the purpose of analysing protocol variation between centres, the two centres where this respondent practiced were combined to represent one centre. When several responses were received from one centre, responses were either merged if responses were consistent, or responses from the clinician performing the procedure (interventionist) were used to represent procedure-specific information for that centre. Consequently, a per-centre analysis could then be performed for the 19 active centres for which survey information was available (Figure 1).

### Frequency of FCA

Overall, most testing centres (13/19, 68%) performed three to four FCA procedures per month. The remaining centres reported performing >10 procedures per month (one centre), five to 10 per month (two centres), one to two per month (two centres), and fewer than one per month (one centre).

## Pre-Testing Considerations

### Pre-procedural preparation

Before performing FCA, all 19 centres requested patients to withhold calcium channel blocker (CCB) therapy. Other medications less frequently withheld included nicorandil (17/19, 89%), long-acting nitrate (17/19, 89%), beta blockers (9/19, 47%), perhexiline (4/19, 21%), and ivabradine (3/19, 16%). Only two centres (10%) withheld angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, or ranolazine. The duration of withholding medications varied, with 11 (58%) centres requesting between 24 and 48 hours and eight (42%) centres requesting at least 48 hours before testing. Most centres (16/19, 84%) recommended avoidance of caffeine before testing, with different withholding periods reported: ≥48, 24, and 12 hours requested by two (11%), nine (47%), and five (26%) centres, respectively.

### Access site and electrocardiographic monitoring

All centres reported the radial or distal radial artery as the preferred access site. A radial artery cocktail was given at

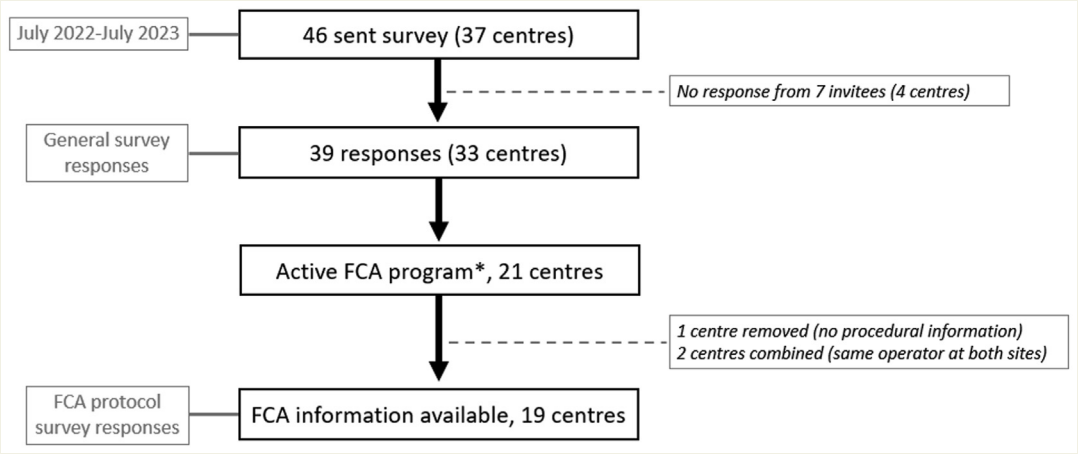


**Figure 1** Flowchart of survey responses. The asterisk denotes an active FCA centre, defined as centres confirming the following: (1) measurement of microcirculatory resistance indices and (2) approved institutional access to acetylcholine for coronary vasomotor testing.
Abbreviation: FCA, functional coronary angiography.

most centres (15/19, 79%) either routinely in every case (6/19) or as required (9/19), most commonly administering nitrate (11/15, 73%), verapamil (6/15, 40%), and heparin (7/15, 47%). Intraprocedural electrocardiographic monitoring was performed most commonly using six leads (12/19, 63%), with only three centres using 12 leads (3/19, 16%) and four centres using another setup.

### ACh access

Of the centres that confirmed institutional access to ACh, 13 (68%) reported unrestricted approval for use, whereas six centres (32%) required a request to the pharmacy for individual patient use.

### Coronary blood flow assessment equipment

All 19 centres had access to a pressure–temperature sensor guidewire (PressureWire X), with five of these centres also having access to Doppler wire (ComboWire). CoroFlow software (Coroventis) was available in 16 of the 19 catheter laboratories, with 10 laboratories integrating Coroventis output onto boom monitors and six laboratories using a standalone laptop.

## Functional Coronary Angiography (FCA) Protocol

### Order of testing

When performing FCA, 53% (10/19) of centres reported measuring hyperaemia resistance indices (IMR/hMR) first, followed by coronary spasm provocation testing. Conversely, 37% (7/19) of centres performed FCA in the opposite order, with the remaining two centres varying their order of testing (Figure 3).

### Rate of ACh administration

When testing vasomotor function, the rate of ACh administration varied significantly among centres: 68% (13/19) of centres used rapid bolus (administered over 20 seconds; spasm provocation) and 21% (4/19) used slow bolus (administered up to 2 minutes; endothelial function test), one centre performed only an infusion (over 2–3 minutes; endothelial function test), and one centre performed both a slow bolus and infusion (Figure 3). These responses suggest that most centres focus on spasm provocation rather than the measurement of endothelial function and endothelial-dependent changes in coronary blood flow.

### Single vs multivessel testing

All testing centres reported that they would first test the left coronary artery (LCA). If LCA testing returned a normal result, six centres routinely proceeded to right coronary artery (RCA) testing in all patients, whereas eight centres only did so for those with a high index of suspicion. Interestingly, one centre routinely tested RCA even if LCA testing provided a positive result, whereas four centres reported that they rarely tested the RCA at all (Figure 3).

### Temporary pacing wire (TPW)

Of the testing centres, 63% (12/19) reported routine use of TPW when performing FCA, most commonly when testing RCA (75%, 9/12). However, two centres also routinely used TPW when testing dominant LCA, and two centres used TPW routinely during the testing of any vessel, including non-dominant LCA. Conversely, seven centres (37%, 7/19) reported no routine use of TPW, even when testing RCA (Figure 3).

## Procedure Timing

### Performing ad hoc FCA

When testing centres were asked whether patients with angina who undergo invasive coronary angiography and are found to have unobstructed arteries should proceed to FCA

**Table 1 Location of the 33 centres that responded to the survey.**

| Centre (n=33) | State, country | Measuring resistance indices | Access to ACh | Active FCA program (n=21) |
|---|---|---|---|---|
| Queen Elizabeth Hospital | SA, Australia | Yes | Yes | Yes |
| Royal Adelaide Hospital | SA, Australia | Yes | Yes | Yes |
| Calvary Adelaide Hospital | SA, Australia | Yes | Yes | Yes |
| University of Adelaide | SA, Australia | No | No | No |
| Lyell McEwin Hospital | SA, Australia | Yes | Yes | Yes[a] |
| Western Health, Melbourne | Vic, Australia | Yes | Yes | Yes[b] |
| Alfred Hospital, Melbourne | Vic, Australia | Yes | Yes | Yes[b] |
| Austin Health, Melbourne | Vic, Australia | Yes | Yes | Yes |
| Peninsula Health, Frankston | Vic, Australia | Yes | Yes | Yes |
| Victorian Heart Hospital | Vic, Australia | Yes | Yes | Yes |
| Northern Health, Melbourne | Vic, Australia | No | No | No |
| Cabrini Hospital, Melbourne | Vic, Australia | Yes | Yes | Yes |
| Gosford Hospital, Central Coast LHD | NSW, Australia | Yes | Yes | Yes |
| Concord Repatriation General Hospital | NSW, Australia | Yes | Yes | Yes |
| John Hunter Hospital | NSW, Australia | Yes | No | No |
| Nepean Hospital | NSW, Australia | No | Yes | No |
| Royal North Shore Hospital | NSW, Australia | No | Yes | No |
| Bankstown-Lidcombe Hospital, Sydney | NSW, Australia | Yes | Yes | Yes |
| Liverpool Hospital | NSW, Australia | Yes | Yes | Yes |
| Royal Prince Alfred Hospital | NSW, Australia | Yes | Yes | Yes |
| Coffs Harbour Health Campus | NSW, Australia | Yes | No | No |
| Wollongong Hospital | NSW, Australia | No | No | No |
| Orange Hospital | NSW, Australia | No | No | No |
| Royal Perth Hospital | WA, Australia | Yes | Yes | Yes |
| Fiona Stanley Hospital | WA, Australia | Yes | Yes | Yes |
| Gold Coast University Hospital | Qld, Australia | Yes | Yes | Yes |
| Sunshine Coast University Hospital | Qld, Australia | No | No | No |
| Canberra Hospital | ACT, Australia | Yes | No | No |
| Royal Hobart Hospital | Tas, Australia | Yes | Yes | Yes |
| Royal Darwin Hospital | NT, Australia | Yes | No | No |
| Auckland City Hospital | New Zealand | Yes | Yes | Yes |
| Wellington Hospital | New Zealand | Yes | Yes | Yes |
| Christchurch Hospital | New Zealand | Yes | No | No |

Centres with active FCA programs were identified as those that responded "yes" to both measuring microvascular resistance indices and confirmed access to ACh.
[a]One centre was removed from analysis of protocol variation, as procedural information was not available.
[b]Two centres were combined for the purpose of pre-centre protocol analysis, as the same operator worked across both sites using the same protocol.
Abbreviations: FCA, functional coronary angiography; ACh, acetylcholine; SA, South Australia; Vic, Victoria; LHD, Local Health District; NSW, New South Wales; WA, Western Australia; Qld, Queensland; ACT, Australian Capital Territory; Tas, Tasmania; NT, Northern Territory.

during the same procedure, 13 of the 19 (68%) testing centres agreed or strongly agreed that ad hoc FCA would be appropriate. However, when asked how often ad hoc FCA was performed in routine clinical practice among suitable patients, only one centre (5%) confirmed that they performed it frequently (50% of the time). Furthermore, four centres stated that they performed it occasionally (20% of the time), and 14 of the 19 (74%) centres stated that they never or rarely performed ad hoc testing, instead preferring to schedule patients for further testing on dedicated coronary physiology lists (Figure 3).

### Myocardial infarction with non-obstructive coronary arteries

Among patients admitted to hospital with presumed myocardial infarction with non-obstructive coronary arteries (MINOCA), most testing centres (14/19, 74%) elected to defer FCA to a later date, either after cardiac magnetic resonance failed to explain diagnosis or if patients experienced further

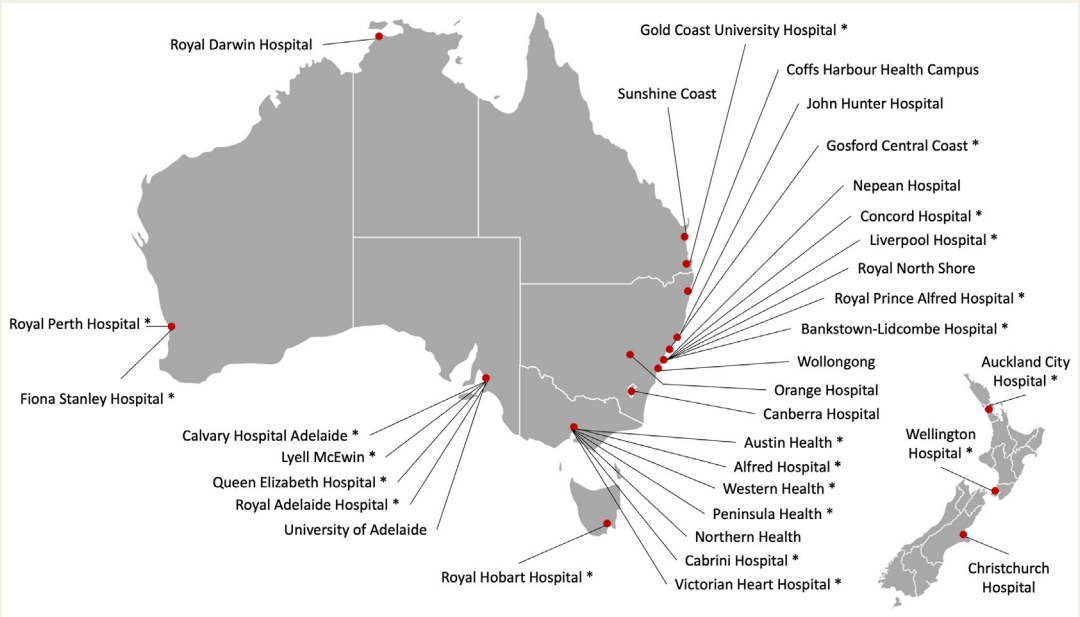


**Figure 2** Location of responding centres within Australia and New Zealand. The asterisk denotes an active FCA centre, defined as centres confirming the following: (1) measurement of microcirculatory resistance indices and (2) approved institutional access to acetylcholine for coronary vasomotor testing.
Abbreviation FCA, functional coronary angiography.

unexplained symptoms, with only three centres (16%) considering that FCA should be offered during index admission.

**Barriers to performing FCA**

Finally, when respondents were asked to identify potential barriers to performing FCA at the time of index angiography, additional time, cost, use of vasoactive medications, and lack of a national (CSANZ) protocol were among the most commonly identified reasons.

# Discussion

To the best of our knowledge, this report represents the first survey-based study conducted across all centres performing FCA within Australia and New Zealand, providing for the first time nationwide insights into the variation in testing protocols used during routine clinical practice.

Our survey reports several key findings. Across Australia and New Zealand, 21 centres were identified as having an active FCA program, with 19 included within our analysis. Among these centres, FCA was performed infrequently despite clinicians reporting that the measurement of comprehensive coronary physiology is useful for clinical management. Access to ACh varied among the centres, with many hospitals requesting access on a named patient basis. Despite general agreement that among appropriate patients, follow-on FCA during index coronary angiography would be helpful, follow-on FCA was seldom if ever performed. Furthermore, among patients with suspected MINOCA, FCA was rarely performed during index admission. This observation may be explained by the need for pre-procedural preparation, with our survey reporting that all centres recommended withholding medications, and most centres required a caffeine-free period pre-testing. However, other barriers to testing included additional cost, catheter laboratory time, and the lack of a national CSANZ protocol.

## Common Protocol Features

Across all testing centres surveyed, complete protocol agreement (100%) was demonstrated for radial artery as the preferred access site, testing of the LCA first, and pre-procedural withholding of vasoactive drugs. Moderate-to-high levels of protocol agreement (90%–60%) were observed for routine administration of radial cocktail (79%), TPW when testing RCA (63%), rate of intracoronary ACh administration (rapid bolus, 68%), and recommendation of a caffeine-free period before testing (84%).

## Protocol Variations

Significant protocol variations were reported. Firstly, recommendations regarding which vasoactive medications should be withheld before testing varied across sites. Whilst all centres recommended the withholding of CCB, many centres also recommended cessation of oral nitrate (89%) or nicorandil (89%), with some centres requesting the withholding of any medication that could potentially influence vasomotor function (beta blockers, alpha blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blocker). Furthermore, the duration of withholding medications varied, with some centres requesting 12 hours and others >48

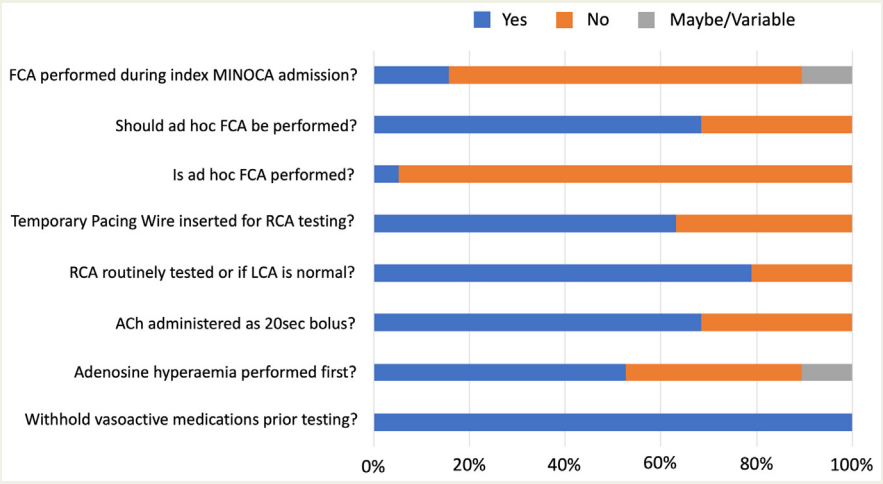


**Figure 3** Responses to functional angiogram survey.
Abbreviations: FCA, functional coronary angiography; MINOCA, myocardial infarction with non-obstructive coronary arteries; RCA, right coronary artery; LCA, left coronary artery; ACh, acetylcholine.

hours. Generally, it is recommended that vasoactive medications be withheld for 24 to 48 hours before testing [3,15], which was the most commonly chosen withholding period among the surveyed centres. Similarly, caffeine may influence response to adenosine [16]; however, not all centres requested a caffeine-free period before testing. The influence of these variations (in the type of medication withheld, duration of withholding medication, and the presence or absence of a caffeine-free period) on FCA results remains unclear.

Secondly, variation in the order of vasomotor testing was evident, with just over half of the centres routinely assessing adenosine-induced hyperaemia resistance indices (IMR/hMR) first and then ACh spasm provocation testing, whereas the remaining centres either used the converse order or varied their order of testing. The influence of variation in the order of testing on the interpretation of results remains unclear. Use of intracoronary nitrates before assessing adenosine-induced resistance indices has been advocated to ensure large vessel vasodilation. Interestingly, administration of intracoronary nitrates among patients with positive ACh provocation tests has recently been shown to prevent vasospastic angina (VSA) on subsequent ACh rechallenge in most patients, particularly those with epicardial spasm [17]. Whilst further research is required to better understand this observation, it seems possible that administration of intracoronary nitrates before ACh testing may reduce diagnostic yield. Conversely, when the order of testing is reversed, abnormalities in microcirculatory resistance and coronary blood flow may persist among patients who demonstrate an abnormal vasomotor response to intracoronary ACh, despite the administration of intracoronary nitrates. This may potentially influence the subsequent measurement of adenosine-induced resistance indices, especially if performed quickly (<3 minutes) after ACh testing [18].

Thirdly, variation in rates of ACh administration was reported. Most commonly, a rapid (20-second) bolus was used (spasm provocation dose). However, nearly a third of centres administered ACh as either a slow bolus or infusion to assess for endothelial dysfunction or impairment of endothelium-dependent changes in coronary blood flow. However, detection of VSA requires a rapid bolus of ACh (typically over 20 seconds), and hence false-negative tests for VSA are possible when only using slow rates [18].

Fourthly, whilst centres uniformly tested LCA first, only a few centres then proceeded to test RCA if LCA test results were within the normal range, stating that they would only do so with patients for whom they had a high index of suspicion. Interestingly, one centre routinely tested RCA even in the presence of abnormal LCA findings, which is consistent with Japanese recommendations [8]. The influence of routine multivessel vs LCA-only testing on diagnostic yield remains unclear. A recent study that involved routine multivessel testing suggested regional variation in microcirculatory resistance within the same participant [19]. If confirmed in further studies, these observations may provide support for routine multivessel testing rather than the frequently adopted left anterior descending (LAD) artery–only approach.

Fifthly, routine TPW use was reported in nearly two-thirds of centres during FCA, with the remaining centres reporting that TPW was not necessary. It may be possible to avoid the use of TPW by simply slowing the rate of ACh infusion if significant atrioventricular block is observed. Whilst this method has been described [14], it remains unclear how intraprocedural variations in the administration rate of ACh influences the sensitivity for the detection of VSA, and therefore the interpretation of results overall.

Finally, despite recent observations suggesting that testing patients with suspected MINOCA during index admission

appears to be safe and significantly adds to diagnostic yield [20–23], FCA among these patients in Australia and New Zealand is seldom performed during their index admission.

## Protocol Variation Within International Expert Consensus Statements

Following recent publications that demonstrate the clinical utility and benefit of FCA [9,10], testing for VSA and coronary microvascular disease is now guideline-recommended and part of routine clinical care [6–8]. However, there remains an absence of an agreed-upon standardised testing protocol. Various expert consensus documents exist, including those from Europe (European Association of Percutaneous Cardiovascular Interventions [EAPCI]) [24], Japan (Japanese Circulation Society) [8], Canada (expert review) [25], and the United States of America (Microvascular Network [MVN]) [26], and provide helpful guidance around testing protocol. However, whilst many similarities exist among these documents, such as the recommendation of withholding vasoactive drugs and caffeine before testing and focusing testing on the LAD initially, several areas of inconsistency and uncertainty are described.

Importantly, major inconsistency exists around the order in which vasoreactivity testing (intracoronary ACh administration) and microcirculatory resistance testing (adenosine-induced resistance indices) should be performed. Both EAPCI [24] and Canadian [25] documents describe performing adenosine-induced resistance testing first, with the caveat that it may be acceptable to reverse the order. Conversely, the MVN [26] states that the order of testing may be at the preference of the operator, while Japanese groups advocate for ACh testing first [8,18,27]. Multivessel ACh provocation is encouraged within Japanese expert documents [8,18], with European and American documents supporting further vessel testing only after LAD test results are demonstrated to be within the normal range and there is a reasonable index of suspicion.

Further inconsistency exists among these documents in the recommendations for dose and rate of ACh administration during vasoreactivity testing. Whilst both Japanese [8] and Canadian [25] documents recommend increasing doses of intracoronary ACh (LCA, 50, 100, and 200mcg; RCA, 20 and 50mcg) administered rapidly (over 20 seconds), the MVN [26] recommend an initial low ACh dose (20mcg) administered slowly (over 2–3 minutes) followed by a larger dose (100mcg) given more quickly (30–60 seconds). The European Association of Percutaneous Cardiovascular Interventions (EAPCI) [24] provides much broader guidance, recommending that a pragmatic approach be adopted by each individual centre based on whichever protocol works best for their hospital, with supplemental material detailing both slow ACh infusion and rapid bolus techniques. UK guidelines [27] are similarly pragmatic, suggesting slow infusion of ACh over 2–3 minutes only if Doppler wire testing is performed. Conversely, without Doppler wire assessment a typical procedure includes assessing CFR/IMR, followed by observing the response to a 100mcg bolus of ACh administered over 20 seconds using angiographic assessment, electrocardiography, and symptom monitoring.

## Urgent Need for Protocol Standardisation

Despite established guideline recommendations, our survey demonstrates that, unfortunately, FCA is performed infrequently and among a relatively small number of centres. This finding may reflect the ongoing general under-recognition and under-diagnosis of patients with suspected ANOCA. Additionally, variation in testing protocols reported across the FCA sites may limit the widespread application of testing, pose difficulties for clinicians in the interpretation of results, introduce complexities in FCA procedural training and confusion in cardiology trainee education, and limit collaborative research in this field. Consequently, there exists a desperate need for standardisation of testing. The CSANZ Coronary Vasomotor Dysfunction Working Group is currently in the process of submitting such a protocol, and it is hoped that widespread adoption of a national protocol will help overcome these barriers and facilitate progress in this clinically and economically important area.

In addition to providing useful insights into routine clinical practice, this survey also provides other benefits. For example, conducting this survey has facilitated the creation of network links between centres active within the area of coronary physiology. Similar to the American MVN [26], we hope that linking centres collaboratively within projects such as the current one may help further expand collaborative research within Australia and New Zealand.

## Limitations

Our survey has several limitations. Firstly, the survey was conducted over a 12-month period; thus, initial respondents may have changed their practice at the time of manuscript submission. Secondly, whilst most centres (89%) responded to the survey, we did not receive data from four centres, which may influence the final results.

Thirdly, our survey did not collect information on other relevant aspects of FCA, such as procedural safety/tolerability of testing, rates of positive results, or selection criteria for testing. Fourthly, our survey did not ask directly what technique had been used to measure coronary blood flow, but instead assumed that coronary blood flow would have been measured using equipment available at that centre. At five centres, equipment for both Doppler and bolus thermodilution techniques was available. Therefore, the proportion of patients who were tested using these two techniques at these centres remains unclear.

Fifthly, our survey did not specifically ask whether centres performed spasm provocation (rapid bolus) or endothelial function testing (slow bolus or infusion), but instead used rate of ACh administration to establish the type of testing performed. Whilst all centres responded that they would either use a rapid bolus or slow bolus/infusion, the survey assumes that these rates of ACh administration reflect the

centres' intention to test for spasm or endothelial dysfunction. Finally, it is possible that the Working Group was unaware of some centres undertaking FCA, although this is unlikely given the nationwide membership of the group.

The CSANZ Coronary Vasomotor Dysfunction Working Group is currently developing a clinical quality registry, which we hope will help to overcome these limitations in the future.

## Conclusions

This survey provides the first nationwide insight into attitudes towards and variation in testing protocols among clinicians and centres performing FCA across the whole of Australia and New Zealand. Importantly, our survey demonstrates significant protocol variations among centres. Whilst comprehensive physiology testing programs are beginning to expand globally, the impact of protocol variation on interpretation of results, training of junior medical staff, and future research remains problematic. Consequently, there is currently an urgent need for a standardised testing protocol which, if adopted widely, may help to mitigate some of these barriers, thus driving innovation, development of novel therapeutics, and further collaborative research within this important area of cardiovascular medicine.

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We report no relevant funding sources associated with this manuscript.

## Conflicts of Interest

The Cardiac Society of Australia and New Zealand (CSANZ) Coronary Vasomotor Dysfunction Working Group is an independent physician-led organisation without any financial relationship to industry. Individual authors have the following relevant disclosures. J.S. has received speaker fees and an unrestricted educational grant from Abbott Vascular. T.J.F. has received speaker fees from Abbott Vascular and Boston Scientific. A.Y. received speaker fees and research support from Abbott Vascular, and research support from Philips. C.Z. has received speaker fees from Abbott Vascular. J.F.B. has no conflicts of interest to disclose.

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Coffs Harbour Health Campus, NSW (Lambert B)
Concord Hospital, University of Sydney, NSW (Yong A)
Fiona Stanley Hospital, Curtin University, Perth, WA (Ihdayhid AR)
Gold Coast University Hospital, Qld (Singh K)
Gosford Hospital, Central Coast Local Health District, NSW (Ford T)
John Hunter Hospital, NSW (Turner S, Al-Omary M)
Liverpool Hospital, Sydney, NSW (Lo S)
Lyell McEwin Hospital, Adelaide, SA (Arstall M)
Alfred RP, Macquarie University, Hospitals, Sydney, NSW (Ng MK).
Nepean Hospital, Kingswood NSW (Khor L).
Northern Health, Melbourne, Vic (Van Gaal W).
Orange Hospital, Orange, NSW (Elder A).
Health, Frankston, Vic (Layland J).
The Queen Elizabeth Hospitals, University of Adelaide, Basil Hetzel Institute, Adelaide, SA (Beltrame JF, Zeitz CJ).
Royal Adelaide Hospital, Adelaide, SA (Worthley M, Lau JK). Royal Darwin Hospital, Darwin, NT (Wing-Lun E).
Royal Hobart Hospital, Hobart, Tas (Adams HSL).
Royal Perth Hospital, Perth, WA (Spiro J, Rajwani A).
Royal North Shore S, NSW (Brieger D).
Sunshine Coast University Hospital. Sunshine Coast, Qld (Sidharta S).
University of Adelaide, Adelaide, SA (Montarello N, Pasupathy S).
Victorian Heart Hospital, Melbourne, Vic (Wong D)
Western Health and Alfred Hospital, Melbourne, Vic (Chan W).
Wellington Hospital, Wellington, NZ (Fairley S). Wollongong Hospital, Wollongong, NSW (Shetty P).

## Appendices

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.hlc.2024.04.299

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