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### Coronary stenosis physiology appraisal

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# CHAPTER 6

## Discordance between pressure drift after wire pullback and intracoronary distal pressure offset affects stenosis physiology appraisal

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## ABSTRACT

### Background

Drift is a well-known issue affecting intracoronary pressure measurements. A small pressure offset at the end of the procedure is generally considered acceptable, while repeat assessment is advised for drift exceeding  $\pm 2$  mmHg. This practice implies that drift assessed after wire pullback equals that at the time of stenosis appraisal, but this assumption has not been systematically investigated. Our aim was to compare intra- and post-procedural pressure sensor drift and assess benefits of correction for intra-procedural drift and its effect on diagnostic classification.

### Methods

In 70 patients we compared intra- and post-procedural pressure drift for 120 hemodynamic tracings obtained at baseline and throughout the hyperemic response to intracoronary adenosine. Intra-procedural drift was derived from the intercept of the stenosis pressure gradient-velocity relationship. Diagnostic reclassification after correction for intra-procedural drift was assessed for the mean distal-to-aortic pressure ratio at baseline (Pd/Pa) and hyperemia (fractional flow reserve, FFR), and corresponding stenosis resistances.

### Results

Post- and intra-procedural drift exceeding the tolerated threshold was observed in 73% and 64% of the hemodynamic tracings, respectively. Discordance in terms of acceptable drift level was present for 42% of the tracings, with avoidable repeat physiological assessment in 25% and unacceptable intra-procedural drift unrecognized at final drift check in 17% of the tracings. Correction for intra-procedural drift caused higher reclassification rates for baseline than hyperemic functional indices.

### Conclusions

Post-procedural pressure drift frequently does not match drift during physiological assessment. Tracing-specific correction for intra-procedural drift can potentially lower the risk of inadvertent diagnostic misclassification and prevent unnecessary repeats.

## INTRODUCTION

Physiologic assessment of coronary stenosis severity has repeatedly been shown to yield superior outcomes compared to angiographic revascularization guidance and intracoronary pressure represents an integral measure for various indices assessed at coronary flow rates ranging from resting to hyperemic conditions<sup>1-4</sup>.

Despite careful adherence to manufacturer instructions and recommended procedural guidelines<sup>5-7</sup>, biological and technological factors can adversely affect repeatability and accuracy of intracoronary pressure measurements<sup>8</sup>. Among the latter, drift of the guide wire pressure sensor has been identified as a common source of error that can lead to diagnostic misclassification and may necessitate re-assessment<sup>9-12</sup>. Besides careful initial conditioning, zeroing, and pressure equalization prior to physiological assessment, a (non-hyperemic) drift check after withdrawing the pressure sensor to the guiding catheter is considered critically important to validate the accuracy of the results<sup>7,8</sup>. A final aortic-to-distal pressure difference (Pa-Pd) within  $\pm 2$  mmHg<sup>9</sup> or a pressure ratio (Pd/Pa) between 0.97 and 1.03<sup>12,13</sup> is arbitrarily considered acceptable even in core laboratory analyses. Repeat normalization and physiological assessment is advised for larger pressure offsets<sup>7,9,14</sup>, although repeating the measurement is no guarantee for absence of drift.

An inherent assumption for these recommended practices is that the post-procedural pressure offset measured after wire withdrawal equals the intra-procedural drift present at the time of physiological lesion assessment. This implies that drift, once present, stays constant for the duration of the procedure. However, this assumption has not been systematically investigated.

It should be recognized that the pressure signal downstream of a stenosis does not convey quantifiable information about possible corruption by intra-procedural drift. Only distal pressure combined with flow velocity provides a means to ascertain sensor inaccuracy during intracoronary assessment based on the well-known pressure gradient-velocity ( $\Delta P$ -v) relationship characterizing stenosis hemodynamics<sup>15-17</sup>. Since physical laws dictate that the pressure gradient across a stenosis must be zero at zero flow, a non-zero  $\Delta P$  intercept of this curve represents the amount of intra-procedural drift<sup>18,19</sup>.

We hypothesized that intra-procedural drift differs from the final pressure offset measured at the end of a procedure. Accordingly, the primary goal of our study was to compare intra- and post-procedural pressure drift. A secondary aim was to evaluate the clinical benefit of correction for tracing-specific drift and to quantify the effect of this correction on diagnostic classification of stenosis severity.

## METHODS

### Data source

We retrospectively analyzed intracoronary measurements obtained between 2001 and 2011 in 70 patients with stable coronary artery disease who were scheduled for elective percutaneous coronary intervention (PCI). All patients were enrolled in study protocols involving multiple invasive physiological assessments in the target vessel pre- and post-revascularization, if performed, and in a reference vessel (defined as <30% diameter stenosis on visual inspection), if present<sup>18, 20</sup>. Exclusion criteria consisted of left main, 3-vessel or diffuse disease, recent myocardial infarction (<6 weeks) in the target vessel perfusion area, severe valvular abnormalities, left ventricular dysfunction (ejection fraction <40%), cardiac arrhythmia, advanced heart failure or prior cardiac surgery. The respective study protocols were approved by the institutional ethics review board and all patients gave written informed consent.

Hemodynamic measurements of acceptable quality were eligible for inclusion when the following events were recorded: initial zeroing of aortic and distal pressure transducer; distal and aortic pressure equalization at the start, and check for pressure drift at completion of the procedure.

### Cardiac catheterization and hemodynamic measurements

Cardiac catheterization was performed via standard femoral approach using a 5F or 6F guiding catheter without side holes. Intracoronary nitroglycerin (0.1 mg) was administered prior to diagnostic angiography and repeated for procedures lasting longer than 30 minutes. Aortic pressure was measured via the guiding catheter, with the pressure transducer fixed at mid-chest level. Coronary pressure and flow velocity were simultaneously measured with a dual sensor-equipped guidewire (ComboWire XT<sup>®</sup>, Volcano Corp., San Diego, CA, USA). After zeroing all pressure systems, the distal pressure signal was equalized to aortic pressure at the tip of the catheter prior to advancing the wire to the measurement location. The ECG and all hemodynamic signals were continuously recorded at rest and throughout the response to an intracoronary bolus of adenosine (20-40 µg). Post-procedural drift was determined after withdrawing the wire pressure sensor to the catheter tip.

### Data analysis

Quantitative angiograms analysis yielded vessel dimensions and diameter reduction (QCA-CMS 5.2, Medis Medical Imaging Systems, Leiden, Netherlands). Hemodynamic signals were extracted from the digital recordings using in-house developed software (AMC Studymanager) and cycle-averaged values of all physiological variables were determined based on the ECG R-wave. The whole-cycle resting and hyperemic distal-

to-aortic pressure ratio (Pd/Pa and FFR, respectively) were derived. Baseline (BSR) and hyperemic stenosis resistance (HSR) were calculated by their respective  $\Delta P/v$  ratio. All indices were averaged over at least 3 consecutive cycles. Thresholds indicating diagnostic significance were Pd/Pa  $\leq 0.92$ , FFR  $\leq 0.80$ , BSR  $> 0.66$  mmHg·cm<sup>-1</sup>·s and HSR  $> 0.8$  mmHg·cm<sup>-1</sup>·s. Pressure drift was considered present when the pressure offset, Pa-Pd, exceeded  $\pm 2$  mmHg.

### Derivation of tracing-specific pressure drift

a) Intra-procedural drift was derived from physical principles of stenosis hemodynamics: 1) there is no pressure difference between two points along a fluid-filled tube when there is no flow and 2) the stenosis  $\Delta P$ -v relation reflects the sum of pressure losses due to viscous friction and flow separation as  $\Delta P = Av + Bv^2$  (i.e.  $\Delta P=0$  when  $v=0$ ), where A and B are coefficients accounting for stenosis geometry and the rheological properties of blood. This well-established quadratic relationship describes the hemodynamic characteristics of an arterial stenosis and holds both for cycle-averaged means and instantaneous values during diastole<sup>15-17, 21, 22</sup>. It has been extensively studied and validated in vitro, in animals, and in humans over the past decades.

b) In order to quantify intra-procedural drift, paired per-beat averages of stenosis  $\Delta P$  and flow velocity at baseline and throughout the hyperemic response were fitted with the quadratic relationship  $\Delta P = Av + Bv^2 + C$  (Grapher vs. 12, Golden Software, CO). The coefficient C is the intercept of this curve fit at zero flow velocity. A non-zero  $\Delta P$  intercept hence represents the tracing-specific intra-procedural drift<sup>18, 19, 23</sup>. Reproducibility of this intercept determination was checked for cases with suitable repeat measurements.

### Correction for tracing-specific drift

Pd was corrected for intra-procedural drift by adding the zero-flow intercept of the pertinent  $\Delta P$ -v curve to the measured value. Diagnostic reclassification of the derived functional indices occurred when corrected values crossed the respective threshold for each index.

Lastly, we also compared drift prevalence assessed by Pa-Pd with the 3% Pd/Pa ratio<sup>12</sup>.

### Statistical analysis

Continuous variables are expressed as mean  $\pm$  SEM unless specified otherwise. Categorical variables are presented as counts and percentages. Normality of data distribution was assessed using the Kolmogorov-Smirnov test. Continuous variables were compared with unpaired Students t-test or one-way ANOVA, as appropriate. Bland-Altman analysis was used to check agreement between corresponding drift values and, together with linear regression, to assess reproducibility of intra-procedural drift determination. Levene's test was used to assess equality of variances for drift differences (post - intra) between

groups. Linear or multinomial logistic regression was used, as appropriate, to examine the effect of study vessel (LAD, LCX, or RCA), vessel type (reference, stenosis or post-PCI measurement), diameter reduction, and elapsed time since initial pressure normalization on intra- and post-procedural drift or their difference. Statistical tests were performed on a per-tracing basis using SPSS vs. 20 (IBM, Armonk, NY). Two-tailed values of  $P < 0.05$  were considered significant.

## RESULTS

Patient demographics, clinical characteristics and angiographic findings are summarized in Table 1. A total of 120 physiological tracings were analyzed. These were obtained in 39 reference, 47 stenosed, and 34 revascularized arteries, with a mean FFR of  $0.85 \pm 0.02$  (Suppl. Figure 1). Post-procedural drift at the catheter tip was measured 89 times, i.e. in 31 cases more than one physiological measurement was obtained before a final drift check.

### Comparison of intra- and post-procedural pressure drift

Figure 1 shows examples of physiology tracings and corresponding  $\Delta P$ -v relationships that illustrate the temporal variability of sensor drift. The top panel was obtained for a 26% stenosis in the left anterior descending artery of a 57 yr old male. In this example, intra-procedural drift exceeding the acceptable range went unnoticed at final drift check, which would inadvertently affect the derived diagnostic indices. Conversely, the outcome obtained for a 73% stenosis in the right coronary artery of a 55 yr old male (bottom panel) revealed a drift of -9 mmHg during the intracoronary measurement, whereas the final pressure offset was 8 mmHg.

In total, unacceptable post-procedural pressure offset after pull-back was present in 72% (64/89) of the pullback measurements, associated with 73% (87/120) of the physiological tracings, while unacceptable intra-procedural drift was detected in 64% (77/120) of the tracings.

Although the frequency distributions were similar for intra- and post-procedural drift assessments (Suppl. Figure 2) corresponding drift appraisals did not match in 42% (50/120) of these cases. As outlined in the discordance overview (Figure 2), intra-procedural drift exceeded  $\pm 2$  mmHg in 17% (20/120) of the tracings while the final pressure offset was within acceptable limits, hence resulting in potential misclassification due to unrecognized drift at the time of physiological assessment. Conversely, for 25% (30/120) of the tracings, the  $\Delta P$ -v intercept showed no evidence of drift whereas the pull-back offset exceeded tolerated limits, thereby prompting unnecessary repeat of normalization and lesion assessment.

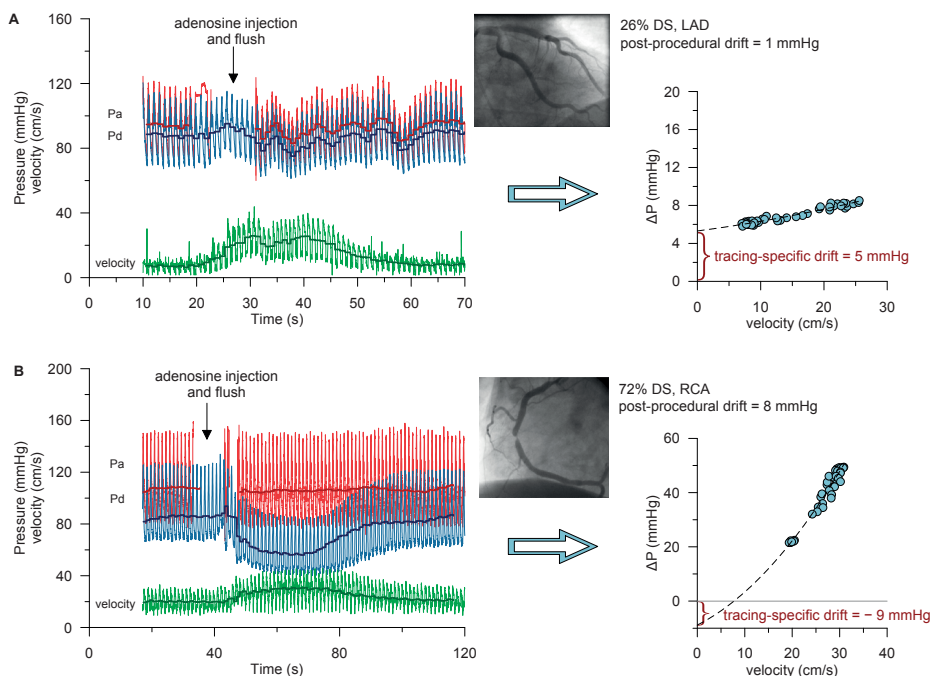
**Table 1.** Patient demographics (n = 70) and stenosis characteristics

Age (years)	58 ± 1
Male sex	55 (79)
Prior myocardial infarction	5 (7)
Coronary risk factors	
Hypertension	26 (37)
Smoking	23 (33)
Hypercholesterolemia	34 (49)
Diabetes	4 (6)
Medication	
ACE inhibitors	13 (19)
Aspirin	65 (93)
β-Blockers	57 (81)
Calcium antagonist	26 (37)
Nitrates	34 (49)
Study vessel (n = 93)	
LAD	41 (44)
LCX	36 (39)
RCA	16 (17)
Diameter reduction (%)	
all (n = 120)	32 ± 2
reference vessels (n = 39)	19 ± 1
stenosis (n = 47)	54 ± 2
post-PCI (n = 34)	13 ± 2
Minimum lumen diameter (mm)	
all (n = 120)	2.1 ± 0.1
reference vessels (n = 39)	2.4 ± 0.1
stenosis (n = 47)	1.3 ± 0.1
post-PCI (n = 34)	2.8 ± 0.1

Values are expressed as mean ± SEM or *n* (%). ACE= angiotensin-converting enzyme, LAD= left anterior descending artery, LCX = left circumflex artery; RCA = right coronary artery; PCI = percutaneous coronary intervention

Neither intra- nor post-procedural drift was significantly associated with study vessel, percent diameter reduction or vessel type (reference vessel, stenosis or post-PCI measurement). Bland-Altman analysis of drift differences revealed no trend or difference in bias for the respective vessel types (1.6 mmHg, 0.3 mmHg, -1.2 mmHg, respectively). However, wide limits of agreement of respectively -7.2 to 10.7 mmHg, -15.6 to 16.2 mmHg, and -12.5 to 10.1 mmHg were found (Suppl. Figure 3) for reference vessels, stenosis, and post-PCI. In particular, drift mismatch tended to increase with lesion severity



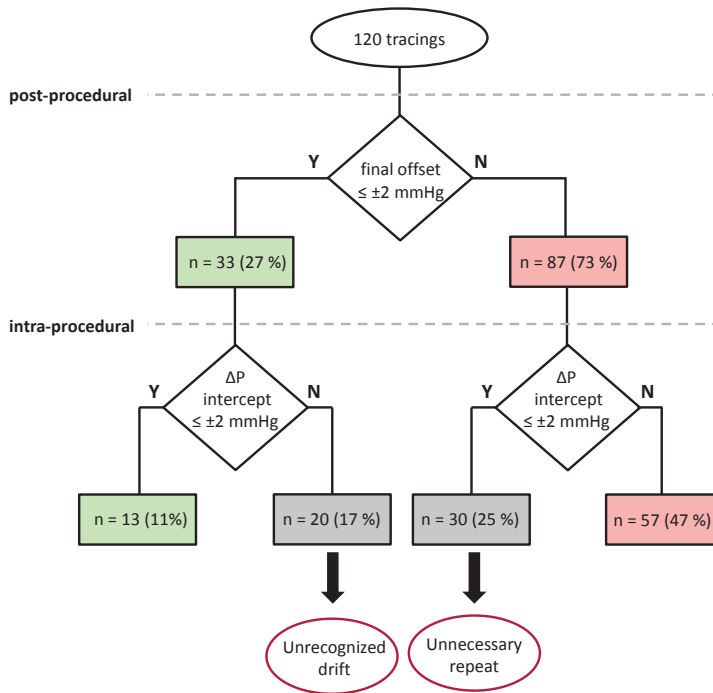


**Figure 1** Examples of aortic pressure (Pa), distal pressure (Pd), and coronary flow velocity ( $v$ ) tracings throughout the response to a bolus of intracoronary adenosine (**left panels**). Cycle-averaged values of pressure gradient ( $\Delta P$ ) and velocity form the basis for the quadratic fit (**right panels**) to derive the intra-procedural drift ( $\Delta P$ - $v$  intercept), as indicated by the circle on the  $\Delta P$  axis. For the first example (**A**), the post-procedural pressure offset was 1 mmHg and hence acceptable, whereas the drift during the physiological assessment was 5 mmHg, thereby unwittingly affecting the derived diagnostic indices for this case. For the second example (**B**), the final pressure offset was 8 mmHg, while the intra-procedural drift was -9 mmHg. For this case, both drift estimates revealed unacceptable drift levels, although drift occurred in two opposite directions. Corresponding angiographic images for the two cases (**A**, **B**) are also shown.

(Suppl. Figure 4) as corroborated by a larger variance ( $p=0.015$ ) and a clearly inflated interquartile range of drift differences (-3.7 to 4.8 mmHg) compared to reference (0.2 to 4.1 mmHg) or revascularized arteries (-3.1 to 1.9 mmHg).

Reproducibility of the derived intra-procedural drift for 46 repeat assessments was excellent, as confirmed by the significant linear relationship ( $y=0.99x - 0.03$ ,  $r^2=0.992$ ,  $p<0.0001$ ), and a bias of 0.03 mmHg with 95% limits of agreement from -0.98 to 1.05 mmHg.

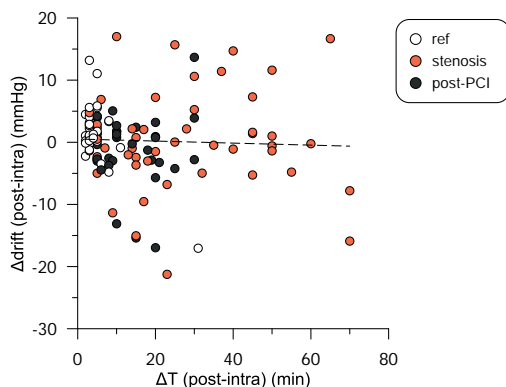
The elapsed time since initial pressure equalization ( $22 \pm 2$  min, median 19 min) was not significantly associated with intra-procedural drift ( $p=0.56$ ). The average time interval between intra-procedural and final drift assessment was  $17 \pm 2$  min (median 10



**Figure 2** Flowchart of agreement between post- and intra-procedural drift. Discordance between post- and intra-procedural drift classification was present in 42% of the tracings. An acceptable residual offset at the end of the procedure while the intercept exceeded  $\pm 2$  mmHg was present for 17% of the tracings, incurring potential drift-induced misclassification. Conversely, when the final pressure offset was not tolerable, the  $\Delta P$  intercept was within acceptable limits for 25% of the tracings, pointing to avoidable repeat assessment.

min), and was significantly shorter for measurements in a reference vessel ( $5 \pm 1$  min) or post-PCI ( $14 \pm 2$  min) than for stenosis assessment ( $28 \pm 3$  min),  $p < 0.001$ . Nonetheless, the difference between intra- and post-procedural drift showed no relation to elapsed time between these two assessments ( $r = 0.06$ ,  $p = 0.51$ , Figure 3).

Using the Pd/Pa ratio as a less stringent measure of final drift yielded similar results. Unacceptable post-procedural drift ( $>3\%$  deviation of Pd from Pa) was present in 53% (47/89) of the ostium measurements. Interestingly, pressure offset and Pd/Pa ratio only agreed in 58% of the total number of tracings in terms of the respective acceptance criteria. In 24 cases (20%), post-procedural drift was acceptable when assessed by Pd/Pa, but not acceptable according to the pressure difference. Notably, aortic pressure was significantly higher for this discordant group compared with the concordant one (106.4 mmHg vs. 97.7 mmHg,  $p < 0.01$ ).



**Figure 3** Differences between post- and intra-procedural drift were not associated with the time interval between the respective measurements ( $r=0.06$ ,  $p=0.51$ ). Pressure drift exceeding tolerated limits was prevalent even for small time intervals < 10 min, whereas acceptable drift was present for time intervals exceeding 50 min. ref=reference vessels, PCI= percutaneous coronary intervention.

### Effect of drift correction on lesion classification

Correction for intra-procedural drift affected the various functional indices to different degrees. In 81 cases (68%) FFR changed by more than its intrinsic test-retest variability ( $\pm 0.02U$ )<sup>24</sup> after drift correction. Owing to the lower pressure gradient at resting flow, drift correction resulted in almost twice the number of re-classifications (17 versus 9) for whole-cycle Pd/Pa than for FFR (Suppl. Figure 5A-B). Similarly, 4 BSR values were reclassified as significant and 14 as non-significant, while 1 HSR value was reclassified as significant and 5 as non-significant after accounting for tracing-specific drift (Suppl. Figure 5C-D).

## DISCUSSION

In this study we compared the pressure offset after final wire pull-back with derived drift at the time of physiological assessment and assessed the effect of tracing-specific drift correction on stenosis classification. Our major findings are: 1) Pressure drift after sensor withdrawal to the catheter tip did not match intra-procedural drift in 42% of the cases. 2) Functional indices of stenosis severity were more susceptible to drift problems when assessed at baseline (Pd/Pa and BSR) than at hyperemia (FFR and HSR). 3) The ensuing risk of unrecognized diagnostic misclassification (17% of the cases) or avoidable repeat of measurements (25% of the cases) can be mitigated by tracing-specific correction for intra-procedural drift based on the zero-flow intercept of the stenosis  $\Delta P$ -v relationship.

### Pressure drift is prevalent for all sensor types

All pressure sensors are subject to drift due to gradual changes in sensitivity. A variety of mechanical, electrical, or environmental influences during regular use can additionally trigger a variable positive or negative shift in the sensor output that affects individual

measurements to varying degrees<sup>9, 25, 26</sup>. Only limited information is available regarding pressure drift in current clinical practice, but the problem clearly exists for all currently used sensor types. Recent studies rarely mention actual drift prevalence or extent. In fact, only drift frequency in terms of an unacceptable Pd/Pa ratio has been reported, ranging from 7.4 to 33% for piezoelectric and from 3.5 to 13% for optical pressure sensors<sup>4, 12-14, 27</sup>. Stated Pd/Pa drift values in one prior study<sup>12</sup> show a slightly smaller range, but a similar distribution as our drift findings. In those studies, every tracing was followed by a mandatory pullback for drift check, which was not the case in the present study, where multiple measurements were obtained before wire withdrawal for a final drift assessment.

### Reasons for drift mismatch

The final pressure offset observed at the catheter tip is commonly assumed to be associated with a slowly worsening performance over time. We did not find a relation of drift development with elapsed time. Instead, intra-procedural drift may be partially reversed when the sensor is withdrawn to the catheter tip, hence accounting for larger 'drift' during than after physiological assessment. This was true for 44% (53/120) of our tracings. Bending stresses on the pressure sensor while negotiating tortuous coronary vessels or passing complex stenotic constrictions may constitute a key factor causing mismatch between intra- and post-procedural drift. In fact, the difference between intra- and post-procedural drift tended to be more pronounced for measurements that were obtained distal to a stenosis compared to reference vessels or post-PCI.

It should be recognized that perceived pressure sensor 'drift' may in part be attributable to changes in the height of the external aortic pressure transducer connected to the fluid-filled guiding catheter<sup>28</sup>. A contribution of hydrostatic pressure changes cannot be accounted for and keeping the aortic pressure transducer at a fixed height, as was done in the present study, is imperative to avoid misinterpretation of final drift values.

### Tracing-specific drift assessment from combined distal pressure and velocity signals

Like a non-zero pressure offset at final drift check, a non-zero  $\Delta P$  intercept at zero flow constitutes a deviation from the initial zeroing and pressure equalization that is attributable to drift. Owing to the relative ease of measurement and supported by technological development efforts of various manufacturers, functional lesion assessment is preferably performed with a pressure wire. However, once the sensor is downstream of a stenosis, a distal pressure deviation resulting from sensor drift cannot be directly measured without comparison to a known reference.

The proposed derivation of intra-procedural drift requires simultaneous pressure and flow velocity measurements. At present, only the Philips-Volcano Combowire is suitable for this purpose. Complementary knowledge of coronary flow velocity allows a more

comprehensive assessment of both epicardial (stenosis) and microcirculatory physiology<sup>29, 30</sup>. Intracoronary flow assessment in addition to coronary pressure also opens new avenues for improved risk stratification and prognosis, especially in intermediate lesions with discordant FFR and coronary flow velocity reserve and in patients with non-obstructive coronary artery disease<sup>21, 31, 32</sup>.

We acknowledge that the proposed method for drift estimation and correction adds complexity to the analysis. Current capabilities in real-time processing permit the online derivation of the stenosis  $\Delta P$ -v relationship and tracing-specific drift correction. The development of appropriate dedicated software indeed represents a desirable improvement in future versions of the instrument console.

### **Clinical impact of tracing-specific drift correction**

Even tolerated amounts of drift have been identified as potential source of error for diagnostic classification<sup>9, 10, 12</sup>, whereas the absence of final drift is commonly regarded as proof of drift-free physiology assessment<sup>7, 8, 12</sup>. The prevalence of discordant drift findings in the present study suggests that reliance on final drift checks may distinctly compromise clinical decision-making. Our results also advise against correcting distal pressure based on final drift assessment<sup>10, 33</sup>. Intra-procedural drift assessment allows correction of acquired distal pressure signals tailored to each tracing, thereby reducing the risk of inadvertent diagnostic misclassification (17% of our cases) and of performing avoidable physiology re-assessments (25% of our cases).

The clinical impact in terms of re-classifications after drift correction obviously depends on the distribution of measured values around the cut-off. In our unselected cohort, only 31% of baseline Pd/Pa values and 15% of FFR values were within  $\pm 0.05U$  of their respective cut-point.

Nonetheless, the higher diagnostic re-classification rate after drift correction confirmed that functional stenosis indices assessed at baseline are more vulnerable to misclassification even in case of small, acceptable drift<sup>9</sup>. This is hardly surprising given the small resting pressure gradients for mild to intermediate lesions, in the order of 4-6 mmHg for the whole cycle and 8-11 mmHg during the wave-free period<sup>22</sup>.

We identified fewer drift cases based on the Pd/Pa ratio than with Pa-Pd, which points to potentially erroneous acceptance of drift-corrupted lesion measurements especially in patients with elevated aortic pressure. This may be even more pertinent for pressure-only indices at resting conditions, considering that control of flow by autoregulatory mechanisms renders stenosis pressure gradients fairly resilient to variations in aortic pressure<sup>34</sup>.

### **Study limitations**

The retrospective nature of this single-center study is a limitation. However, this was a mechanistic investigation with hypothesis-generating findings that warrant further ex-

ploration in a larger patient cohort with combined pressure and velocity measurements. The ongoing DEFINE-FLOW trial (NCT02328820) could provide this opportunity.

Extensive physiological protocols with multiple measurements in the studies comprising our data pool may be a reason for the relatively high drift prevalence in our study. However, this does not account for the frequent drift mismatch which essentially puts into question the reliability of a final drift check as a gatekeeper to ensure measurement accuracy.

Inaccurate flow velocity assessment can theoretically contribute to a faulty  $\Delta P$  intercept at zero flow. In the present study, reliable measurements of flow velocity were achieved by careful positioning of the Doppler sensor. The goodness of the quadratic fit corroborates the physiological reliability of the velocity measurements to yield  $\Delta P$ -v relationships consistent with stenosis hemodynamics in humans<sup>17, 18, 23, 35</sup>.

Although the flow response to our comparatively low dose of IC adenosine was likely within 10% of maximal flow<sup>36</sup>, this may have affected the binary diagnostic classification in borderline cases. However, this does not alter our main findings regarding discrepancies between intra- and post-procedural drift, as maximal flow is not needed to reliably assess pressure drift from the intercept of the  $\Delta P$ -v curve<sup>18</sup>.

It should be recognized that tracing-specific correction of distal pressure measurement error does not reduce diagnostic uncertainty of FFR associated with co-existing cardiac pathologies.

We could not assess the instantaneous pressure ratio during the wave-free period (iFR), but would expect similar outcomes for reclassification after drift correction as for the whole-cycle Pd/Pa.

## Conclusions

Drift occurs frequently during intracoronary physiological assessment and may be overestimated or remain unrecognized when pressure offset is only checked at the end of the procedure. Our results suggest that tracing-specific correction for intra-procedural drift can avoid unnecessary hemodynamic re-appraisal and lower the risk of diagnostic misclassification, with associated benefits in terms of procedure time, patient comfort and cost. Evaluation in a prospective study would be required to further validate these findings.

## Conflict of interest

There was no industry involvement in any aspect of this study. MS received institutional research support from the University of Texas Health Science Center at Houston (for DEFINE-FLOW, NCT02328820). JJP has served as speaker at educational events organized by St Jude Medical, Boston Scientific, and/or Philips-Volcano, manufacturers of sensor-equipped guidewires. The other authors report no conflicts of interest.

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none

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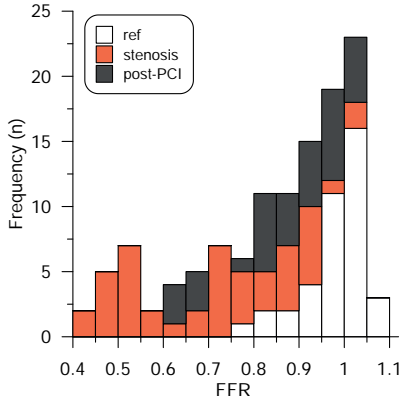
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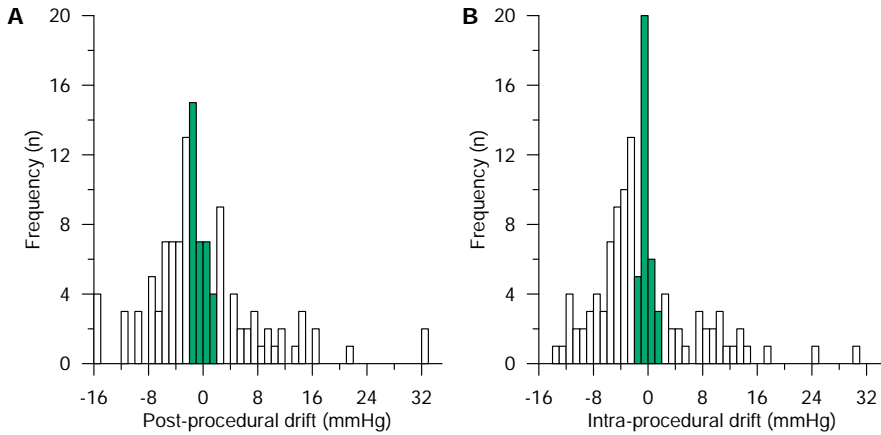
**SUPPLEMENT TO: Casadonte et al., Discordance between pressure drift after wire pullback and intracoronary distal pressure offset affects stenosis physiology appraisal**

**SUPPLEMENTARY FIGURES**

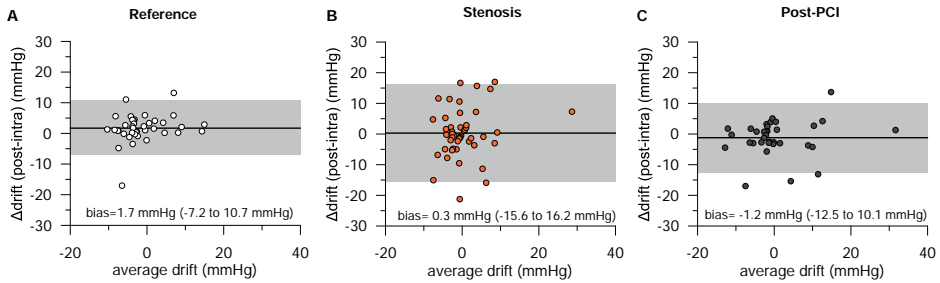


**Suppl. Figure 1** Stacked histogram of the distribution of fractional flow reserve (FFR) values before drift correction, separated by reference vessel, stenosis and post-PCI measurements.

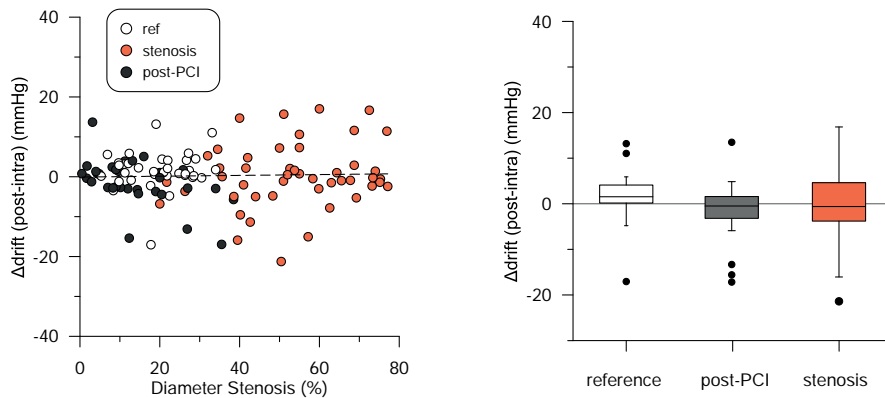
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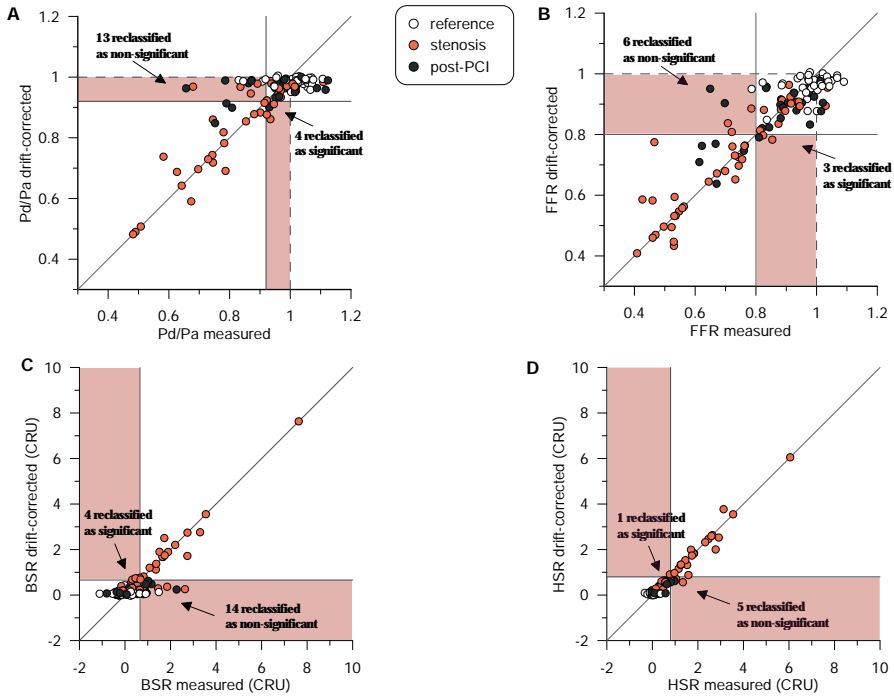
**Suppl. Figure 2** Both range and distributions were similar for post- (A) and intra-procedural drift (B). Green bars indicate acceptable limits of  $\pm 2$  mmHg.



**Suppl. Figure 3** Bland-Altman plots showing the disagreement between final drift check (post) and drift during physiology assessment (intra). Despite similar mean bias, wider limits of agreement between drift differences are evident for stenosis measurements (**B**) compared to reference vessels (**A**) and after revascularization (post-PCI, **C**).



**Suppl. Figure 4** Relations of drift differences (post – intra) to lesion severity. Differences between post- and intra-procedural drift were not associated with percent diameter stenosis ( $r=0.02$ ,  $p=0.81$ ) (**A**). Box plot showing the median and interquartile range of the drift differences separated by vessel type (**B**). Although median drift differences were small ( $<1.6$  mmHg) across all groups, a substantial spread is evident for measurements in the stenosis group (**A**, **B**).



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**Suppl. Figure 5** Classification agreement before and after drift correction. Resting whole-cycle Pd/Pa (A) and BSR (baseline stenosis resistance) (C) were more susceptible to reclassification after correction for intra-procedural drift than FFR (B) and HSR (hyperemic stenosis resistance) (D), respectively. Note that re-classification was not limited to stenosis assessment, but also affected reference and revascularized vessels (post-PCI).