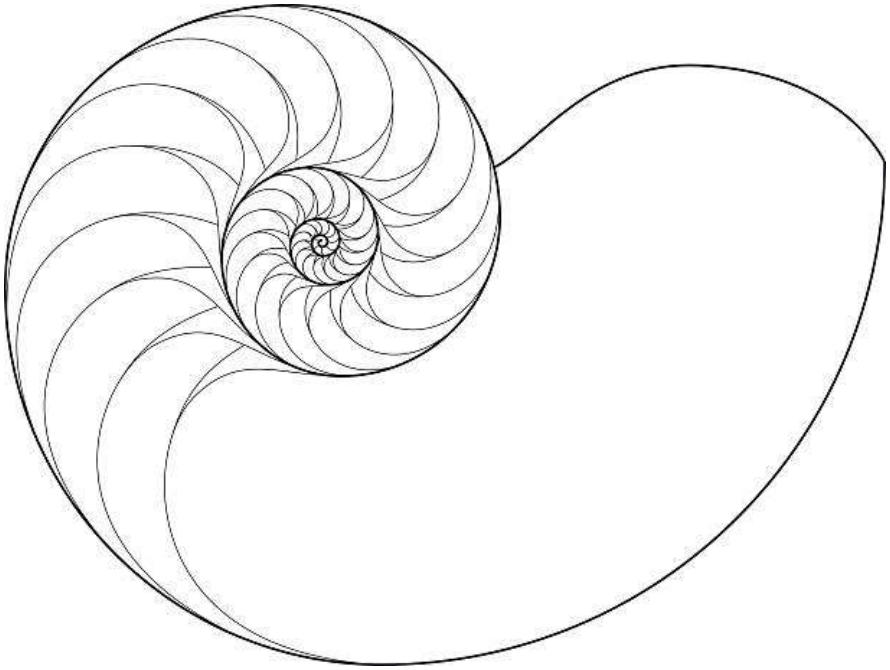
“International PhD program in Cardiovascular Pathophysiology and Therapeutics – CardioPaTh”

Curriculum: interventional cardiology



INTERVENTIONAL CARDIOANGIOLOGY: FROM COMPLEX TO SIMPLE

“From complications of structural and peripheral interventions to detection of coronary artery diseases”

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INTERVENTIONAL CARDIOANGIOLOGY: FROM COMPLEX TO SIMPLE

"From complications of structural and peripheral interventions to detection of coronary artery diseases"

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CHAPTER 1

Introduction

To understand what our next 5 years will look like in the cathlab, I think it is important to review how we came to where we are today. Interventional cardiology may well be one of the most explosive disciplines in the history of medicine. It is one of the rare practices that strives to obsolete itself at warp speed. What's new and innovative today is gone tomorrow, as the next greatest innovation replaces it. I oftern marvel at how hard industry must work to come up with the next generation of what appears to be a perfectly acceptable device. Notwithstanding research in intervantional cardiology couldn't be limited to new devices, drugs and techniques. Sometimes redefining a pathological entity, like for example coronary artery ectasia (CAE) could be extremely useful in order to correctly classify the several degrees of such coronaropathy and consequently identify a standardized therapeutical approach.

1. Structural interventions and their complications

Aortic valve replacement (AVR) has been the mainstay of treatment of symptomatic severe aortic stenosis. The role of transcatheter aortic valve implantation (TAVI; also known as transcatheter AVR or TAVR) as an alternative to surgical aortic valve replacement (SAVR) is evolving. Through both rapidly increasing clinical experience and progressive improvement in TAVI devices (eg, lower profile systems to reduce vascular complications), TAVI outcomes have improved. Ongoing studies continue to scrutinize the risks of TAVI complications and continuing efforts seek to minimize these risks.

Complications of TAVI will be considered in this topic commencing with immediate or periprocedural complications, which are usually apparent during or shortly after the procedure and moving to longer-term considerations. This topic will deal with periprocedural complications related to vascular access (including injury at the arterial access site, arterial tree trauma, and problems with vascular closure), valve deployment (including improper positioning, coronary compromise and annular rupture), valve function (including paravalvular leak), organ injury (including stroke, myocardial ischemia/injury, and acute kidney injury), and arrhythmic complications (including high degree heart block and atrial fibrillation) and late complications including aortic regurgitation and prosthetic valve thrombosis.

2. Peripheral arterial disease

Peripheral arterial disease (PAD) refers to partial or complete occlusion of one or more non-coronary arteries that leads to compromised blood flow and ischemia. Numerous processes are involved in arterial stenosis, however, atherosclerosis remains the most common etiology.

Remarkable technological advances in the past decade, along with patient preference, have shifted revascularization strategies from traditional open surgical approaches toward lower-morbidity percutaneous endovascular treatments. The availability of stents, more than any other advance, has fueled the growth of catheter-based procedures by improving the safety, durability, and predictability of percutaneous revascularization.

Carotid artery stenting (CAS) is considered to be a reasonable alternative to carotid endarterectomy (CEA), particularly in patients at high risk for CEA. Also about lower limbs revascularization, several new devices and techniques, like drug-coated balloons, drug-eluting stents and directional atherectomy came up in last years.

The performances of all these devices as well as their application to different anatomical settings is surely another interesting research field.

3. Coronary arteries and their diseaseas

Coronary field is probably the oldest one in interventional cardiology both in terms of practice and research. Although the latter is focusing more on

drugs, devices and imaging, in recent years also coronary physiology and physiopathology are a hot topic. But why forget normal and pathological coronary anatomy? Coronary artery ectasia (CAE) or coronary artery aneurysm is the aneurysmal dilatation of coronary artery. This condition has been defined as a dilatation with a diameter of 1.5 times the adjacent normal coronary artery based on CASS registry in 1983. This definition, which was proposed well before standardized quantitative coronary analysis (QCA) was developed, raises multiple issues and has so far negatively impacted our understanding about the prevalence and the clinical significance of this pathological condition.

The current working definition impedes the diagnosis in patients with diffuse CAE in whom no reference diameter exists. These patients are not infrequent in practice. Moreover, the absence of reference normal coronary diameters against which establishing the diagnosis, forces interventional cardiologists to diagnose CAE only in the presence of self-evident and full-blown cases. Although the clinical significance of CAE is not fully understood, largely due to under-recognition and the lack of a workable diagnostic algorithm, many studies have demonstrated that it is not a benign disorder and it is associated with a high risk of (recurrent) coronary events. In general, the absence of a specific treatment for these patients has led to systematic under recognition of the importance of this condition.

Under these premises, we should aim at establishing reference values for coronary arteries at invasive coronary angiogram by analysing with QCA a large cohort of healthy individuals who underwent invasive coronary angiogram for suspected, but not confirmed, coronary artery disease who present with uneventful cardiovascular clinical history, no established cardiac disorder, including valvular or muscle heart disease and without established atherosclerosis risk factor.

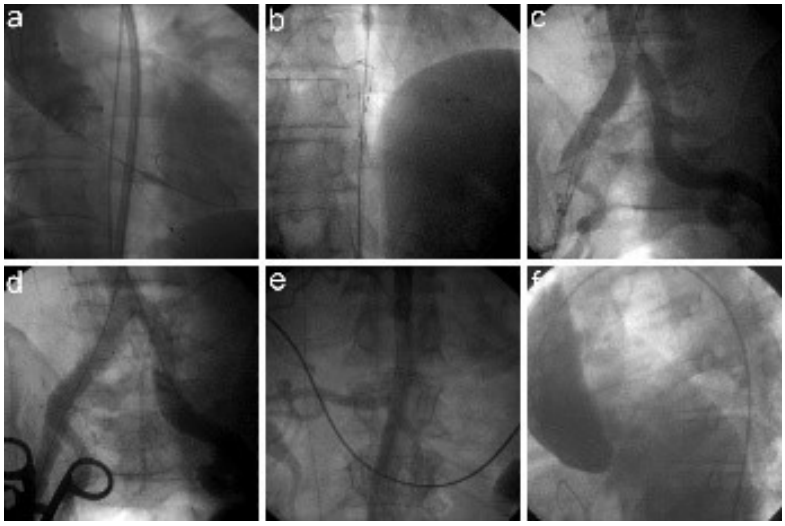
PART 1

Structural interventions and their complications

CHAPTER 2

Acute aortic dissection during ineffective attempt of transcatheter implant of a fully resheathable, respositionable and retrievable aortic valve

Aortic injury is a rare but severe complication that may occur during transcatheter aortic valve implantation (TAVI). Few patients with type A dissection are treated surgically because of the high rate of postoperative mortality and neurological complications in this high-risk population; thoracic endovascular aortic repair is rare too, and technically challenging because of the anatomical variations of spiral type A aortic dissection. Sometimes a watchful waiting strategy could be the best solution. We have reported the case of an acute, extended aortic type A dissection occurred during a TAVI procedure, probably due to the rupture of the dedicated sheath, and conservatively managed.



Multiple fluoroscopies. Pop-out of an aortic bioprosthesis Direct Flow Medical®, after ineffective attempt to implant it (*a*); bioprosthesis retrieval through its specific dedicated basket (*b*); rupture of the sheath probably due to its overdistension after the engagement of the retrieval basket (*c*); angiographic control after surgical extraction of all the transcatheter device, followed by endoprosthesis and covered stent implantation (*d*); final aortographies: iatrogenic acute aortic dissection from pre-carrefour tract of abdominal aorta, with exclusion of the left kidney (*e*) and retrograde extension till ascending aorta, without an evident proximal tear (*f*).

CHAPTER 3

Feasibility and safety of early discharge after Transfemoral transcatheter aortic valve implantation – rationale and design of the FAST-TAVI registry

Background. There is an increasing trend towards shorter hospital stays after transcatheter aortic valve implantation (TAVI), in particular for patients undergoing the procedure via transfemoral (TF) access. Preliminary data suggest that there exists a population of patients that can be discharged safely very early after TF-TAVI. However, current evidence is limited to few retrospective studies, encompassing relatively small sample sizes.

Methods. The Feasibility And Safety of early discharge after Transfemoral TAVI (FAST-TAVI) registry is a prospective observational registry that will be conducted at 10 sites across Italy, the Netherlands and the UK. Patients will be included if they have been scheduled to undergo TF-TAVI with the balloon-expandable SAPIEN 3 transcatheter heart valve (THV; Edwards Lifesciences, Irvine, CA). The primary endpoint is a composite of all-cause mortality, vascular-access-related complications, permanent pacemaker implantation, stroke, re-hospitalisation due to cardiac reasons, kidney failure and major bleeding, occurring during the first 30 days after hospital discharge. Patients will be stratified according to whether they were high or low risk for early discharge (≤ 3 days) (following pre-specified criteria), and according to

whether or not they were discharged early. Secondary endpoints will include time-to event (Kaplan–Meier) analysis for the primary outcome and its individual components, analysis of the relative costs of early and late discharge, and changes in short- and long-term quality of life. Multivariate logistic regression will be used to identify factors that indicate that a patient may be suitable for early discharge.

Discussion. The data gathered in the FAST-TAVI registry should help to clarify the safety of early discharge after TF-TAVI and to identify patient and procedural characteristics that make early discharge from hospital a safe and cost-effective strategy.

CHAPTER 4

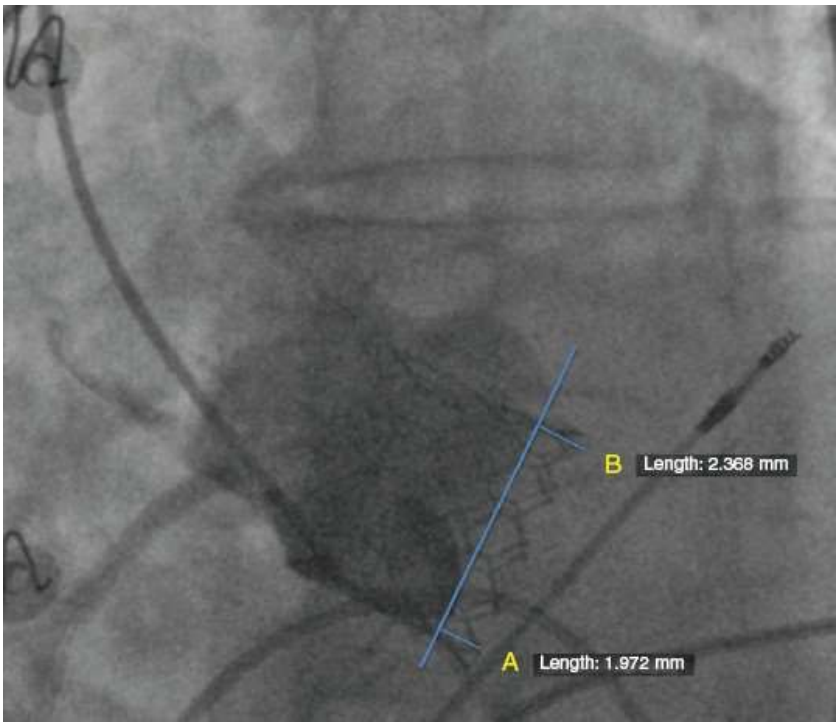
Prosthesis depth and conduction disturbances after last generation balloon-expandable transcatheter aortic valve

Preliminary data on Sapien 3 valve (S3-THV) use for transcatheter aortic valve implantation have shown an increased permanent pacemaker implantation (PPMI) rate with respect to Sapien XT valve. Aim of this study was to investigate the role of S3-THV position in the left ventricular outflow tract (LVOT) on electrocardiographic changes suggestive of atrioventricular (ΔPR) and/or intraventricular conduction abnormalities and 30 days PPMI rate.

Eighty-six consecutive patients treated with S3-THV were included in the study. All patients underwent clinical and electrocardiogram evaluation. Left ventricular outflow tract prosthesis depth was assessed by fluoroscopy and expressed quantitatively (mm) and as aorto-ventricular ratio (AVR).

Eight patients (9.3%) needed PPMI at 30 days. A low AVR (≤60/40) predicted PPMI (OR = 6.09, 95% CI 1.19–31.01, p = 0.030) and resulted into higher PPMI rate, compared with higher AVR (30.0 vs. 6.6%, p = 0.017). For each millimetre increase in the LVOT prosthesis depth PPMI risk increased by 1.41 times (95% CI 1.06–1.87, p = 0.017). In patients with low AVR, ΔPR was higher than in those with higher AVR (33.4 ± 56.7 vs. 12.1 ± 19.4 ms, p = 0.021) and ΔPR was associated to LVOT prosthesis depth (β = 0.286, p =

0.009). Furthermore, ΔPR was associated with risk of PPMI (OR = 1.03, 95% CI 1.01–1.06, p = 0.024).



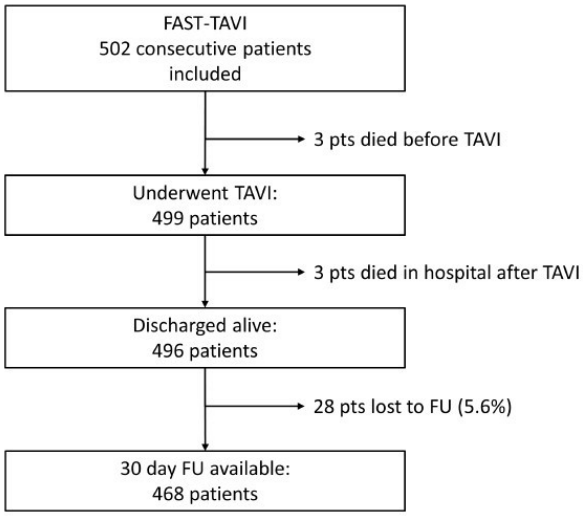
A low AVR is associated to higher ΔPR and PPMI rates. The correlation between LVOT prosthesis depth with ΔPR and higher PPMI rate suggests the need of a careful S3-THV implantation.

CHAPTER 5

Optimizing patient discharge management after transfemoral transcatheter aortic valve implantation: the multicenter european FAST-TAVI trial

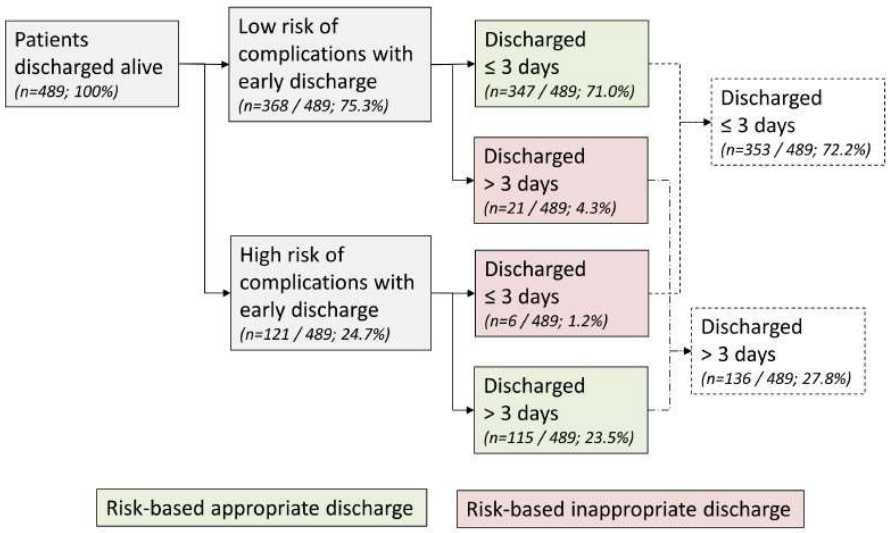
Aims. Treatment pathway optimization in TAVI should include timely patient discharge with a minimized risk for out-of-hospital adverse events.

Methods and Results. We defined and validated the adequacy of a set of discharge criteria and their ability to properly predict timely and safe discharge after the intervention in a prospective, European, multicentre registry. 502 unselected patients were enrolled at 10 sites in 3 countries.



The primary endpoint defined as a composite of all-cause mortality, vascular-access-related complications, permanent pacemaker implantation, stroke, re-hospitalisation due to cardiac reasons, kidney failure and major bleeding at 30

days was reached in 12.9% of patients (95%CI 11.3-16.5). The overall 30-day mortality was 1.1% (95%CI 0.2-2.0), and the rates of stroke/TIA 1.7% (95%CI -0.6 to 4.0), PPI 7.3% (95%CI 5.8-8.9), major vascular complications 1.9% (95%CI 0.7-3.1), major/lifethreatening bleeding 2.4% (95%C 1.0-3.8) and cardiac rehospitalisation 3.7% (95%CI 1.4-6.0). Patients appropriately discharged early had a significantly lower risk of the primary endpoint (7.0 vs. 26.4%; $p < 0.001$) which was reflected in some of its relevant components: stroke (0.0 vs. 2.8%; $p = 0.015$), PPI (4.3 vs. 15.9%; $p < 0.001$), major vascular complications (0.3 vs. 4.7%; $p = 0.004$) and major / life-threatening bleeding (0.3 vs. 6.5%; $p < 0.001$).



Conclusions. We validated the appropriateness of a pre-specified set of risk criteria that allow for a safe and timely discharge. The rate of 30-day

complications did not reveal any risk increase with this strategy compared with the reported outcomes in major TAVI trials and registries.

CHAPTER 6

Invasive electrophysiological evaluation for conduction delays prediction in last generation balloon-expandable TAVI

TEXT

The occurrence of atrioventricular (AV) and intraventricular (IV) conduction disturbances is still common after transcatheter aortic valve implantation (TAVI) and may lead to early permanent pacemaker implantation (PPMI); this represent one of the biggest limitations to the extension of the indication to intermediate-risk patients. A number of patient-related and procedure-related factors, including evidence of conduction system dysfunction, either pre-existing right bundle branch block (RBBB) or AV block occurring at procedural time, valve type, prosthesis oversizing, increased septal wall thickness, and extensive calcification in the area of the non-coronary aortic cusp and/or left ventricle outflow tract (LVOT), have been recognized as being related to the risk of AV conduction defects requiring PPMI after TAVI. After preliminary findings that SAPIEN 3 Transcatheter Heart Valve (S3-THV) (Edwards Lifesciences Inc., Irvine, California, USA) use was associated with increased PPMI rate compared with SAPIEN XT valve (XT-THV) (17.0 vs. 11.0%) [1], a recent study confirmed the suggestion that a more aortic deployment may reduce the need for PPMI, defining 4.26 mm as a “safe” cut-off implantation depth in the LVOT with a PPMI risk increased

by 1.41 times for each mm increase in the prosthesis depth [2]. Aims of this study were to investigate the effects of TAVI with S3-THV on AV and IV conduction by electrophysiological study (EPS), and to individuate new potential predictors of such conduction disturbances.

The study was approved by the "Campania Nord" Institutional Ethic Review Board (approval date 20/01/2016, registry number: CECN/376); all patients gave informed written consent for the procedures. A total of 48 consecutive patients with symptomatic aortic stenosis (25 males, mean age 81.3±4.4 years, mean logistic EuroSCORE 15.7 ± 10.3%, mean STS score mortality 24.9 ± 9.0%) but without previous or new-onset atrial fibrillation or previous PPMI, underwent TAVI with the S3-THV at "Montevergine" Clinic, Mercogliano, Italy, between February and November 2016. All patients underwent high-quality Multi-Detector Computed Tomography (MDCT) angiography evaluation of annulus sizing, as well as leaflets and LVOT calcium score (CS), using a software specifically customized to valve analysis (3mensio Valves™, version 4.1). If possible, the THVs were selected in a narrow sizing range of –5% (undersizing) to +10% (oversizing). According to previous literature findings, all the S3-THV had an "aortic deployment" with more than 60% of the prosthesis implanted above the virtual ring. EPS was performed immediately before the initial balloon aortic valvuloplasty (BAV) and immediately after S3-THV implantation, recording the main standard

parameters, i.e. Atrial-His (AH), His, His-Ventricle (HV), Wenckebach AV block point (WP) and Atrial-Ventricular Node Functional Refractory Period (AVNFRP). No patients received medications likely to have potential effect on the conduction system. ECG monitoring was performed during the procedure and continued for at least 72 h. Intra and periprocedural events were defined according to the Valve Academic Research Consortium (VARC) 2 standardized criteria [3]. PPMI with class I or class IIa indication have been performed according to current guidelines [4]. Statistical analyses were performed using SPSS 16.0 (IBM,…, USA) and MedCalc 13.0. Continuous variables were expressed as absolute numbers and percentage or mean ± SD. Comparisons have been made by the paired or unpaired t test, as appropriate, in the case of normal distribution, or the Wilcoxon or Mann-Whitney U test, as appropriate, in the case of non-normal distribution. Categorical variables have been presented as counts and percentages and compared using Fisher's exact or chi-square test, as appropriate. Univariate and multivariate logistic regression analysis have been performed to identify independent predictors of conduction disturbances detected by EPS. A two-sided p value of < 0.05 will be considered of statistical significance.

A total of five patients (10.4%) needed PPMI after TAVI at 30 days follow-up. No EPS variables resulted significantly prolonged after valve deployment, but in those patients who needed PPMI, ΔHV (80.2 ± 128.5 vs. 8.9 ± 11.2; P

< 0.001) and ΔWP (132.0 ± 198.3 vs. 29.7 ± 45.1; P = 0.005) were significantly longer. Notwithstanding ΔHV and ΔWP did not result associated with leaflets and LVOT CS as well as % prosthesis oversizing.

The close anatomical relationship between the branching AV bundle and the aortic valvular complex provides an explanation for the observed increase in AV or IV disturbances after TAVI. Most changes occur as direct effects on the infra-Hisian conduction system, probably caused by direct pressure on the lower area of the prosthesis on the basal portion of the ventricular septum and the area involving the His-bundle. At present time there is no way to determine the likelihood of recovery or progression of conduction disorders after TAVI therefore, identifying a subgroup of patients with a high probability of developing a high-grade block, which might require PPMI during follow-up, is of the utmost importance. The only study which analyzed the effect of TAVI with balloon-expandable valves on the conduction system by performing an EPS, showed that HV interval and WP were significantly prolonged after XT-THV implantation, but these conduction problems recovered before discharge [5]. According to the safer more aortic implantation technique, in our study the PPMI rate was comparable to XT-THV one (10.4%). Moreover, differently from Eksik findings, ΔHV and ΔWP used as early markers of conduction disturbances as well as new predictors of PPMI, so much so that

deriving data from EPS could provide to the valve team useful informations about the correct timing to safely remove the temporary PM.

According to EPS evaluation, TAVI with S3-THV does not cause significant prolongation of AH, His, HV, WP, AVNFRP, also if HV and WP prolongation significantly predict PPMI. Moreover, a lower implantation depth in the LVOT provides a not different total PPMI rate from that reported for other balloon-expandable valves, independently from prosthesis oversizing and valvular complex calcification amount.

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CHAPTER 7

Impact of contrast mean osmolality on the risk of contrast-induced nephropathy after transcatheter aortic valve implantation

ABSTRACT

Background and aims. Acute kidney injury (AKI) after transcatheter aortic valve implantation (TAVI) is frequent and associated with adverse outcomes and mortality. Aim of the present study was to investigate the relationship between contrast agent osmolality and periprocedural AKI during TAVI.

Methods and Results. From 2011 to 2016, 412 consecutive patients not in dialysis treatment who underwent TAVI for symptomatic severe aortic stenosis (188 males, mean age 80.7 ± 5.8, mean logistic EuroSCORE 17.7 ± 13.8%) were enrolled. According to osmolality of the different iodinated contrast agents (CAs) used for the procedure, the population was divided in 2 groups: iso-osmolality contrast agent (IOCA group, n = 230) and low-osmolality contrast agents (LOCA group, n = 182). Preoperatively, 175 (42.5%) patients suffered from chronic kidney disease (eGFR < 60 mL/min), 98/230 (42.6%) in IOCA vs. 77/182 (42.3%) in LOCA group (p = 0.951). However, a significant difference in postprocedural change of eGFR in IOCA group vs. LOCA group (+3.78 ± 17.27 vs. -3.09 ± 14.87 mL/min, respectively; p < 0.001). Furthermore, a lower percentage of patients developed any stage

of AKI in IOCA group (18/230, 7.8%) vs. LOCA group (21/182, 11.5%), although not statistically significant ($p = 0.201$). Importantly, at linear regression analysis, the use of IOCA resulted the only variable associated with increase in eGFR (beta 0.206, $p < 0.001$), and the association remained even when the amount of CA applied intraprocedurally, logistic EuroSCORE and blood transfusions were included in the multivariable model (beta 0.215, $p < 0.001$).

Conclusions. Strategies to prevent AKI in TAVI patients remain an important challenge. In this study we found that the use of IOCA have a favorable impact on renal function with respect to other CAs and thus should be considered especially for TAVI patient at higher risk for AKI.

INTRODUCTION

Transcatheter aortic valve implantation (TAVI) for high-risk and inoperable patients with severe aortic stenosis (AS) is an emerging procedure in cardiovascular medicine. The applications of TAVI are also expanding to "off-label" indications in patients with intermediate risk, AS secondary to bicuspid valve disease, aortic regurgitation, aortic valve-in-valve procedures, and mitral valve interventions [1]. Little is known of the impact of TAVI on renal function.

Patients undergoing TAVI nowadays are commonly very old and have a high prevalence of chronic kidney disease (CKD). Both the European System for Cardiac Operative Risk Evaluation (EuroSCORE) and the Society of Thoracic Surgeons (STS) score include renal function parameters to evaluate the risk of mortality in cardiac surgery. In fact, trying to avoid potential deterioration of renal function in patients with CKD has become an important argument for choosing TAVI rather than surgical aortic valve replacement in those cases. TAVI procedures involve the administration of contrast agent (CA), the systematic occurrence of short periods of extreme hypotension (rapid pacing, balloon valvuloplasty, and valve deployment), the manipulation of large catheters in the aorta of patients with a high prevalence of diffuse atherosclerosis with the risk of cholesterol embolization, and sometimes the occurrence of paravalvular aortic regurgitation with a reduction in diastolic

renal blood flow: all of them are potential risk factors for acute kidney injury (AKI).

The use of different definitions of AKI (based on the RIFLE [Risk of renal dysfunction, Injury to the kidney, Failure of kidney function, Loss of kidney function, and End-stage kidney disease], VARC [Valve Academic Research Consortium]-1, and VARC-2 criteria), patient and procedural characteristics may explain the disparate incidences across the several series. A meta-analysis including 5,971 patients treated with TAVI shows that AKI occurred in 22.1% of patients and that those with AKI had a significant increase of early and 1-year all-cause and cardiovascular mortality, myocardial infarction, life-threatening bleeding, need for transfusion and dialysis [2]. In 2012, the VARC standardized the timing for the AKI diagnosis, extending from 72 hours to 7 days following a TAVI procedure [3]. With these standardized criteria, Thongprayoon et al reported the incidence of AKI within 7 days following TAVI of 28% (22% in stage 1, 2% in stage 2, and 4% in stage 3) and the need for renal replacement therapy (RRT) during hospitalization of 3% [4]. Actually, compared to patients without AKI, patients who developed AKI after TAVI had a higher mortality rate of 9-44% at 30 days and 32-56% at 1 year [5] [6]. Moreover, in the meta-analysis of Elhmidi et al, a higher preoperative SCr concentration, blood transfusion and peripheral vascular disease are independent predictors of AKI after TAVI [6]. The association between AKI and higher (four-fold) postoperative mortality following TAVI,

was independent of baseline risk profile characteristics and peri-procedural complications [7], suggesting that AKI is a marker for multiorgan failure and is therefore associated with a higher mortality rate. The mechanisms of the growth in morbidity and mortality are: (1) fluid retention with AKI, (2) metabolic acidosis and cardiac dysfunction, and (3) arrhythmia caused by electrolyte imbalance.

Despite their potential to induce acute tubular necrosis, the impact of CA utilization on AKI after TAVI remains controversial. A few studies suggest an association between CA amount and higher AKI incidence following TAVI [8] [9], especially in patients with pre-existing CKD [10], but a recent meta-analysis has shown just a trend toward major CA received in AKI patients [2]. However, another meta-analysis [11] as well as other reports have not demonstrated such association [7] [12] [13] [14] [15] [16]. Minimization of the contrast dose during TAVI to < 100 mL and use of IOCA or LOCAs can explain these observations [8] [13] [17] [18].

Yamamoto et al assessed that the ratio of CA volume x serum creatinine (SCr)/body weight (BW) > 2.7 and CA volume/creatinine clearance (CCr) > 3.7 for predicting AKI could be considered threshold values to decrease the risk of AKI during TAVI [8]. However, for increased levels of SCr, estimated Glomerular Filtration Rate (eGFR) must be approximately 50% decreased. Thus, by the Cockroft-Gault formula, CCr might be calculated higher than it should be; the accuracy of eGFR calculation is higher for impaired or normal

kidneys. For the evaluation of contrast induced AKI development, the CA volume/eGFR ratio can be assumed as a more reliable parameter than the CA volume/CCr. According to Gul et al, the CA volume/eGFR ratio which may predict the development of contrast induced AKI was determined as 3.9 (AUC 0.773, 95% CI 0.604–0.906, sensitivity 71%, specificity 80%) [19].

Hyperosmolality of CA may play a role in the pathogenesis of contrast-induced AKI by causing relatively greater degrees of intra-renal vasoconstriction, activating tubuloglomerular feedback, or increasing tubular hydrostatic pressure, all of which could result in decreased GFR and worsening medullary hypoxemia [20] [21] [22]. A common assumption in many trials has been that, in keeping with the NEPHRIC study [23], iodixanol is a safer agent, at least in those at higher risk of contrast induced AKI, such as those with CKD due to diabetes mellitus. Such iso-osmolal contrast agent (IOCA) was demonstrated to be associated with less nephrotoxicity compared with higher osmolal CAs commonly in use [24]. Notwithstanding the findings of Biondi-Zoccai et al. suggest that there is no difference between iodixanol and low-osmolal contrast agents (LOCAs) like iomeprol, iopamidol and ioversol, being associated with similar absolute risks of contrast induced AKI or ≥ 25% increase of in SCr, and also having comparative odds ratios. [25].

Focusing the effect of contrast osmolality in TAVI cohorts, two studies had shown that the type of CA, IOCA or LOCA, had no influence on the occurrence of AKI [8] [26].

In this observational retrospective study, we compared the incidence of AKI after TAVI in patients receiving IOCA vs. LOCAs. Additionally, we assessed the relationship between the occurrence of TAVI-induced AKI and short-term mortality, and investigated predictors for the occurrence of AKI following TAVI, particularly trying to define new predictive threshold values of the three ratios involving CA volume administered.

MATERIALS AND METHODS

Study population

Between March 2011 and July 2016, a total of 459 consecutive patients diagnosed with symptomatic severe AS underwent TAVI at the "Montevergine" Clinic (115 patients, three operators), Mercogliano, Italy, at the "Santa Maria" Clinic (299 patients, two operators), Bari, Italy, and at the Policlinico University Hospital (45 patients, one operator), Bari, Italy. Patients in chronic hemodialysis treatment as well as patients who died within the 72 hours precluding SCr measurements following TAVI were excluded from the study. Patients who received iodinated CAs within 5 days prior and 72 hours after TAVI, e.g. for Computed Tomography (CT), angiography, Percutaneous Coronary Intervention (PCI), were excluded from the analysis too, thus the final study population consisted of 412 patients.

Details on the TAVI procedure are provided elsewhere [27]. The following devices were used for implantation: SAPIEN XT and SAPIEN 3 (Edwards

Lifesciences, Irvine, CA, USA), CoreValve®, Engager® and CoreValve® Evolute R™ (Medtronic Inc., Minneapolis, MN, USA), JenaValve (JenaValve, Munich, Germany), Acurate and Acurate Neo (Symetis, Ecublens, Switzerland), and finally Direct Flow Medical (Direct Flow Medical® Inc., Santa Rosa, CA, USA).

In diabetic patients on metformin treatment, this drug was suspended 48 hours before TAVI. All patients had an overnight hydration before the procedure: 1 mL/kg/h of 0.9% NaCl solution for 24 hours, at a rate of 60 to 100 mL/hour (according to the individual left ventricular function, pulmonary artery pressure, and combined valvular disease), beginning 12 hours before the scheduled procedure); such isotonic saline solution was implemented for 24 hours before TAVI to the patients with eGFR < 50 mL/min/1.73 m^2.

The number of rapid pacing runs, the occurrence of any complication leading to severe maintained hypotension, and/or the need for hemodynamic support (aortic counterpulsation balloon and extracorporeal circulation) were recorded. Periprocedural events and device success were defined according to the VARC-2 standardized criteria [28]. Follow-up at 30 days was carried out by clinical outpatient visits. Re-hospitalizations for all causes and heart failure were recorded during the follow-up period. Physicians responsible for the patients were contacted and/or medical charts were reviewed to determine the causes of re-hospitalization and/or death when necessary.

All clinical, echocardiographic, procedural, and post-procedural data were prospectively gathered through dedicated archiving software used by each center. The study protocol was in accordance with the institutional ethics committee of each participating center as well as the Declaration of Helsinki, and all patients gave informed written consent for the procedures.

CAs assessment

The CAs used for the procedure were: (1) iodixanol (Visipaque™®, GE healthcare, Little Chalfont, United Kingdom), iodinated non-ionic iso-osmolality, dimeric, (2) iopromide (Ultravist™®, Bayer Healthcare, Berlin, Germany), (3) iobitridol (Xenetix™®, Guerbet, Villepinte, France), (4) iohexol (Omnipaque™®, GE healthcare, Little Chalfont, United Kingdom) and (5) iomeprol (Iomeron™®, Bracco Imaging, Konstanz, Germany), all iodinated non-ionic low-osmolality, monomeric. According to osmolality of the different CAs, the population was divided in 2 groups: IOCA group (n = 230) (iodixanol 320: 290 mosmol/kg H_2O) and LOCA group (n = 182) (iopromide 300-370: 590-770 mosmol/kg H_2O; iobitridol 350: 915 mosmol/kg H_2O; iohexol 350: 780 mosmol/kg H_2O; iomeprol 350: 618 mosmol/kg H_2O).

According to the previous investigations, the CA volume x SCr/BW, CA volume/CCr and CA volume/eGFR ratios were used to evaluate the degree of CA dose in individual patients [8] [19].

The cumulative CA exposure for preoperative CT scan, catheterization, and TAVI has not been taken into account because the time interval to TAVI was more than 5 days for all patients enrolled.

Assessment of renal function and AKI definition

SCr level was measured at baseline (1 day before the procedure), on the procedure day (after continuing the overnight hydration), and then daily until the discharge. SCr concentrations before TAVI were available in all patients. If there was > 1 measurement post-TAVI available, the greater SCr value within 48 hours was included in the analysis. Patients were monitored for at least 72 hours for urine output.

eGFR was calculated with the simplified Modification of Diet in Renal Disease (MDRD) formula [29], while CCr rate using Cockcroft-Gault formula. For the present analysis, CKD was defined as baseline eGFR of < 60 mL/min/1.73 m^2.

AKI was defined as stage 1, 2, or 3 according to VARC-2 [28] following Acute Kidney Injury Network (AKIN) classification [30]. Patients receiving RRT were considered to meet stage 3 criteria irrespective of other criteria. The indications for RRT included fluid overload with heart failure, hyperkalemia, hypercalcemia, metabolic acidosis, uremic symptoms, and oliguria or anuria (urine output < 200 mL/12 hours or urine output < 50 mL/12 hours, respectively).

Risk factors and endpoints

Preoperative risk-related variables were defined according to the EuroSCORE definitions and outcomes were reported according to VARC-2 definitions [28]. Primary study endpoints is to investigate the relationship between contrast agent osmolality and the occurrence of any change in renal function or any grade of periprocedural AKI during TAVI, as well as to identify potential new AKI predictors or to confirm those already mentioned in the literature.

Secondary endpoints to identify potential new AKI predictors or to confirm those already mentioned in the literature.

Tertiary endpoints are: all-cause mortality, cardiac death, stroke, myocardial infarction, cumulative major adverse cardiac events (MACE) at 30 days, cumulative early safety and procedural success [28], congestive heart failure requiring hospital re-admission, but also intravalvular and paravalvular aortic regurgitation, and prosthetic valve dysfunction, evaluated according to the integrative approach outlined in the algorithm advocated by current guidelines [31].

Statistical analysis

Statistical analyses were performed using SPSS 16.0. Variables were expressed as absolute numbers and percentage or mean ± SD. Comparisons were made by t-test, $\chi 2$ test or z-test as appropriate.

Univariate and multivariate logistic regression analysis were performed to identify independent predictors of AKI development. All statistical tests were two-sided. For all tests, a p-value < 0.05 was considered statistically significant.

Baseline characteristics of the study population (n=412).

	Number	Percentage or mean (SD)
Age (yrs)		80.7 (5.8)
Male	188	45.6
Body Mass Index (kg/m^2)		27.6 (4.8)
Hypertension	376	91.3
Diabetes mellitus	142	34.5
Dyslipidemia	210	51.0
Smoking	17	4.1
Chronic kidney disease (eGFR < 60 ml/min/1.73m^2)	175	42.5
eGFR (ml/min/1.73m^2)		67.8 (26.3)
Anemia	217	52.7
COPD	134	32.5
Neurological dysfunction	37	9.0
Severe liver disease	17	4.1
PAD	102	24.8
Porcelain aorta	13	3.2
Critical preoperative state	30	7.3
PM/ICD/CRT implantation	42	10.2
Previous MI	69	16.7
Previous cardiac surgery	70	17.0
Previous myocardial revascularization	108	26.2
PCI	55	13.3
CABG	28	6.8
PCI+CABG	25	6.0
Myocardial revascularization for TAVI	60	14.6
PCI	57	13.8
CABG	2	0.5
PCI+CABG	1	0.2
Coronary artery disease (≥50%) during TAVI	61	14.8
Bridge valvuloplasty	8	1.9
NYHA functional class III-IV	363	88.1
Logistic EuroSCORE		17.67 (13.84)
STS score (mortality)		5.41 (4.33)
Echocardiography		
LVEF (%)		53.6 (12.0)
Maximum aortic gradient (mmHg)		76.2 (21.7)
Mean aortic gradient (mmHg)		47.1 (14.4)
Indexed aortic valve area (cm^2/m^2)		0.39 (0.18)

Moderate to severe mitral regurgitation	180	43.7
Pulmonary arterial systolic pressure (mmHg)		39.6 (13.3)
Electrocardiography		
Heart rhythm		
Sinus rhythm	319	77.4
History of paroxysmal atrial fibrillation	48	11.6
Atrial fibrillation / flutter	66	16.0
PM-induced rhythm	27	6.6

SD = standard deviation; PPMI = permanent pacemaker implantation; COPD = chronic obstructive pulmonary disease; PAD = peripheral artery disease; PM = pacemaker; ICD = implantable cardioverter-defibrillator; CRT = cardiac resynchronization therapy; MI = myocardial infarction; PCI = percutaneous coronary intervention; CABG = coronary artery bypass grafting; TAVI = transcatheter aortic valve implantation; NYHA = New York Heart Association; STS = Society of Thoracic Surgery; LVEF = left ventricular ejection fraction.

Procedural features and outcomes (n=412).

	Number	Percentage or mean (SD)
CT-guided procedure	389	94.4
Vascular access route		
Transfemoral	371	90.0
Transapical	35	8.5
Transaortic	6	1.5
Valve-in-valve	9	2.2
Predilation valvuloplasty	298	72.3
Postdilation	39	9.5
Contrast used (ml)		177.6 (68.2)
Device success	354	85.9
Hospital length of stay (days)		5.7 (5.1)
Any complication (VARC-2)	171	41.5
PPMI	41	10.0
Access site-related complic.	65	15.8
Vascular complications	70	17.0
Minor	57	13.8
Major	13	3.2
PCD failure	34	8.3
Bleeding	84	20.4
Minor bleeding	33	8.0
Major bleeding	45	10.9
Life-threatening bleeding	6	1.5
Need of transfusion	44	10.7
1 unit	24	5.8
2 units	17	4.1
>2 units	3	0.7
Residual AR ≥ moderate	32	7.8
Myocardial infarction	3	0.7
New-onset LBBB	97	23.5
New-onset AF/flutter	35	8.5
Any AKI	39	9.5
AKI 1	29	7.0
AKI 2	7	1.7
AKI 3	3	0.7
Haemodialysis	4	1.0
Chronic hemodialysis	1	0.2
Stroke	4	1.0

Periprocedural death	7	1.7
30-day mortality	15	3.6

SD = standard deviation; PPMI = permanent pacemaker implantation; PCD = percutaneous closure device; AR = aortic regurgitation; AF = atrial fibrillation; LBBB = left bundle branch block; AKI = acute kidney injury.

Patients characteristics by groups.

VARIABLE	IOCA group	LOCA group	p
Patients (n: 412)	230	182	
Age (yrs)	80,45 ± 5,78	80,94 ± 5,91	0,396
Diabetes % (n)	35,65 (82)	32,97 (60)	0,642
Arterial Hypertension %	87,83 (202)	95,60 (174)	0,009
Euroscore II (n)	10,51 ± 51,36	6,86 ± 7,25	0,356
STS Score (n)	3,94 (2,74-6,39)	4,32 (3,25-6,55)	0,064
AKI (n)	7,83 (18)	11,54 (21)	0,268
ΔeGFR ml/min *(post-pre TAVI)*	3,78 ± 17,27	-3,09 ± 14,87	0,002
ΔeGFR ml/min (1 week)	6,41 ± 19,45	1,10 ± 13,92	0,002
Transfusions (n)	0,14 ± 0,53	0,22 ± 0,69	0,178
PAD (n)	35,22 (81)	27,47 (50)	0,116
Ratio 1 (vol x sCR/w)	2,97 ± 1,5	2,48 ± 1,4	<0,001
CKD pre-TAVI	42,61 (98)	42,31 (77)	0,969
Iodio ratio (mg)	935,97 ± 481,74	803,12 ± 557,87	0,010

Post-TAVI AKI predictors.

	Univariate p value	Multivariate p value
CA kind	0,169	
Isosmolality	0,204	0,057
CA volume	0,358	
Diabetes	0,582	
Transfusions (n)	<0,001	0,090
PAD	0,100	
Ratio 1 (vol x sCR/w)	<0,001	0,085
CKD	0,031	

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PART 2

Peripheral arterial disease

CHAPTER 8

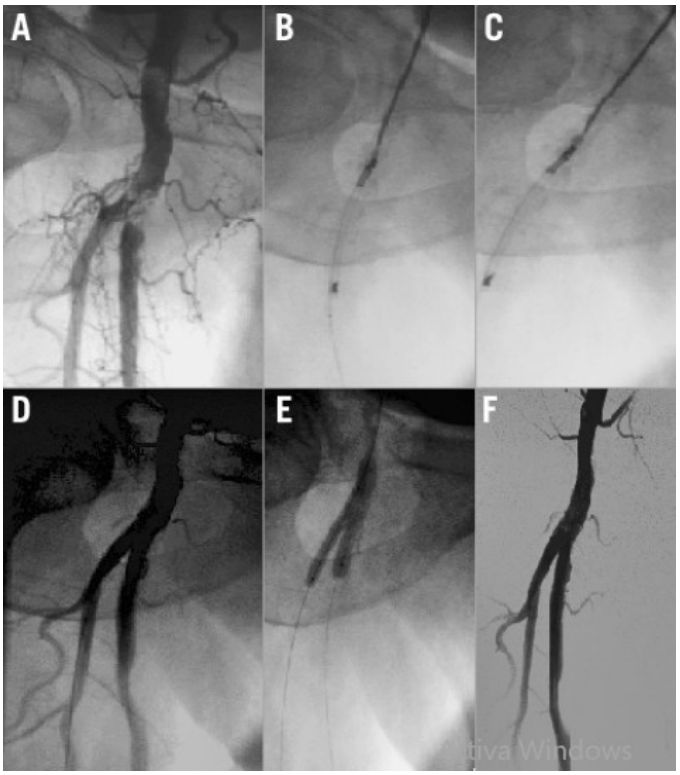
Combined use of directional atherectomy and drug coated balloon for the endovascular treatment of common femoral artery disease: immediate and one-year outcomes

Aims. Surgical endarterectomy is the therapy of choice for atherosclerotic common femoral artery (CFA) obstruction. Recently, some large single-centre series have shown encouraging results for the percutaneous treatment of CFA obstructions. The purpose of this study was to evaluate the safety, feasibility, and one-year efficacy of the endovascular treatment of CFA obstructions with combined use of directional atherectomy (DA) and a paclitaxel-coated balloon (DCB).

Methods and Results. Between January 2012 and July 2014, 30 consecutive patients with severely calcified obstructions of the common femoral artery were treated in our centre using DA followed by DCB dilatation. Provisional stenting was allowed in the case of a suboptimal result. Twenty cases (66%) were isolated CFA interventions, whereas five (17%) and five (17%) also involved inflow and outflow vessels, respectively. Chronic total CFA occlusions (CTO) were recanalised in six cases (20%). Procedural success was achieved in all cases; stenting was needed in three cases (10%). At one year, restenosis and target lesion revascularisation were observed in two of 30

(6.6%) and one of 30 (3.3%) patients, respectively. The secondary patency rate was 96.7%.

Conclusions. This single-centre prospective study suggests that the combined use of DA and DCB is a safe and effective alternative to surgery, a treatment option for common femoral artery lesions and provides encouraging results in this setting.



Treatment of complex common femoral artery obstruction using directional atherectomy and drug-coated balloon. (*a*) Selective angiography showing a calcific obstruction of the distal CFA involving the ostium of both the superficial femoral artery (SFA) and the profunda femoral artery (PFA). (*b*) Use of directional atherectomy to debulk the segment CFA-SFA. (*c*) Use of directional atherectomy to debulk the segment CFA-PFA. (*d*) Selective angiography showing optimal plaque removal after directional atherectomy. (*e*) Simultaneous drug-coated balloon dilation. (*f*) Selective angiography showing final result.

CHAPTER 9

Incidence and predictors of acute kidney injury in patients undergoing to proximal protected carotid artery stenting

Aims. Many studies have analysed the occurrence of acute kidney injury (AKI) after percutaneous coronary intervention (PCI) but there are limited data relating to AKI risk in patients undergoing carotid artery stenting (CAS). The aim of this study was to determine the incidence and predictors of AKI in patients undergoing proximal protected CAS.

Methods and Results. We analysed 456 patients undergoing proximal protected CAS. A binomial multivariate logistic model was developed including patients' clinical and angiographic/procedural characteristics. AKI (defined as an sCr increase ≥ 0.3 mg/dl or ≥ 1.5-fold sCr increase from baseline or more than 50% increase from baseline, within 48 hours post procedure) occurred in 155 patients (34%). AKI patients were more frequently affected by hypertension, diabetes, dyslipidaemia and anaemia, and presented lower renal function at baseline. Higher contrast volume to creatinine clearance ratio (2.40 ± 1.44 vs. 2.08 ± 1.15; p = 0.01), lower post-procedural mean arterial pressure (MAP) (94.3 ± 17.7 vs. 99.6 ± 18.5 mmHg; p = 0.003) and a more frequent post-procedural systolic pressure drop (ΔSBP >50 mmHg) (23.9% vs. 14.3%, p = 0.01) were observed in the AKI group of

patients. At multivariate analysis, independent predictors of AKI were ΔSBP > 50 mmHg, diabetes mellitus and dyslipidaemia.

Conclusions. AKI can occur quite frequently after proximal protected CAS and is related to clinical and procedural features. These data should be confirmed in larger registries or randomised trials.

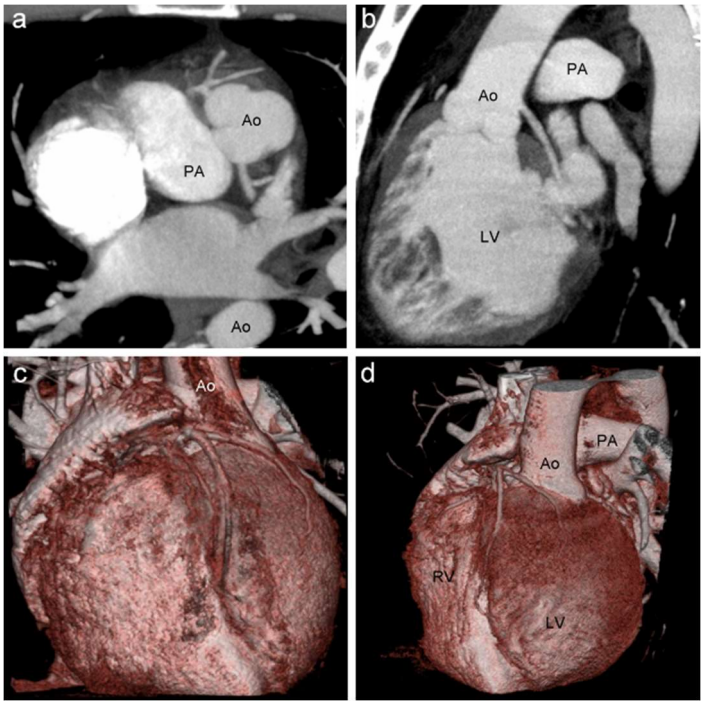
PART 3

Coronary arteries and their diseases

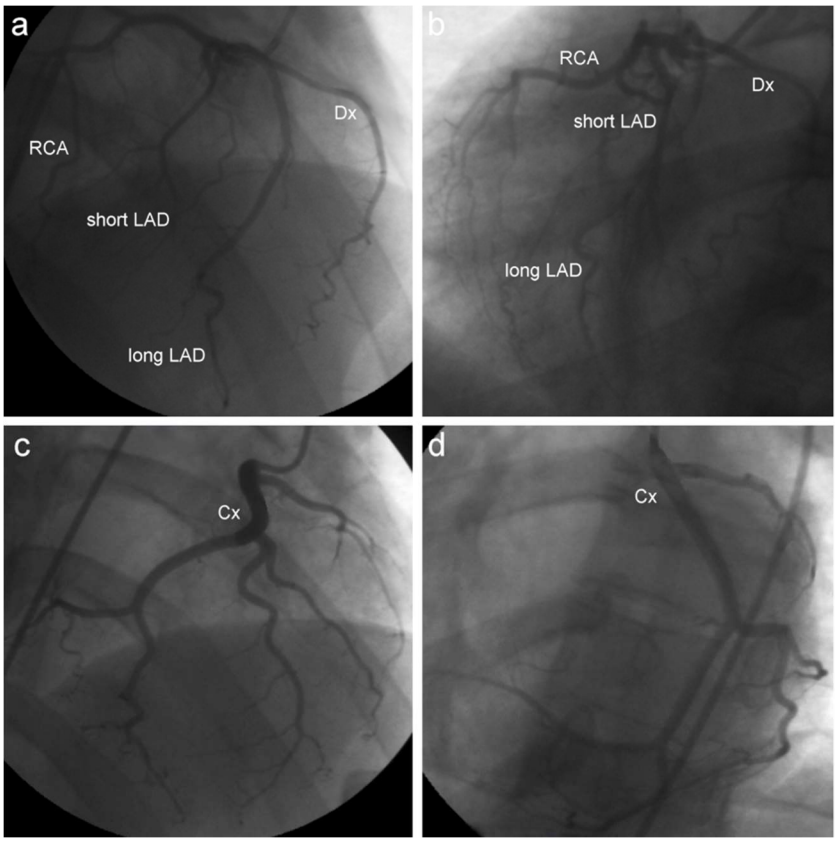
CHAPTER 10

A striking coronary artery pattern in a grown-up congenital heart disease patient

Left ventricular non-compaction (LVNC) is a myocardial disorder, which is thought to occur due to the arrest of normal embryogenesis of the left ventricle (LV), leading to distinct morphological characteristics in the ventricular chamber. The affected segments had a two layer structure: a compact epicardial layer and an endocardial layer consisting of a prominent trabecular meshwork and deep intertrabecular spaces; these features are found predominantly in the apical and the mid ventricular segments of the LV.



It is classified in isolated NC and in ventricular NC associated with other extracardiac and cardiac abnormalities, including coronary artery anomalies.



The prevalence varies considerably among different series and is still unknown; several limitations for this assessment are the different diagnostic criteria, the heterogeneous populations, and the retrospective design of most studies. Because of continuous improvement of imaging resolution quality, this cardiomyopathy is increasingly diagnosed, also if it remains frequently misdiagnosed especially in the cases of LVNC associated with other heart defects. Clinical signs are variable, ranging from lack of symptoms to heart

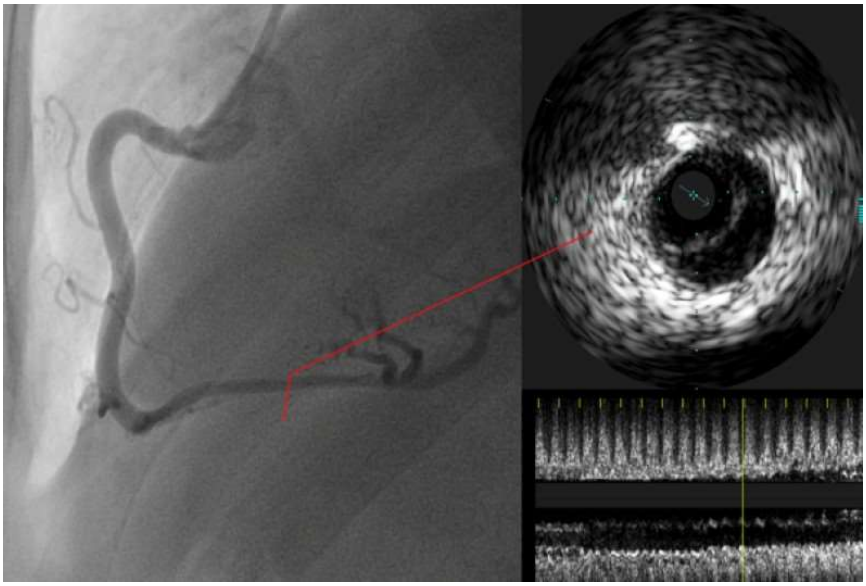
failure, thromboembolic events, arrhythmias till sudden cardiac death, also if the pathophysiologic mechanisms of these severe manifestations in LVNC are partially unclear.

We have presented a case of LVNC association with both malposition of the great arteries and a very original coronary pattern.

CHAPTER 11

How to approach a spontaneous coronary artery dissection: an up-to-date

Spontaneous coronary artery dissection (SCAD) is a separation of the coronary wall layers, not related to trauma, medical procedures or atherosclerosis. The dissection causes the blood entry in the vascular wall with the consequent formation of a false lumen and intramural hematoma. Two pathogenetic mechanisms have been proposed to explain SCAD: a “primary” rupture of coronary endothelium or the rupture of the “vasa vasorum”. Clinical presentation and severity of manifestations are variable, ranging from complete absence of symptoms to acute coronary syndrome, cardiogenic shock, cardiac arrest or sudden cardiac death. Despite coronary angiography is the first-line examination, by supplying two-dimensional images of the lumen, it does not always allow an incontrovertible diagnosis of SCAD. New intravascular imaging techniques, such as optical coherence tomography and intravascular ultrasound, have been recently introduced and may be extremely helpful in assessing the coronary wall integrity, thus improving coronary angiography diagnostic accuracy.



Because of the lack of large randomized trials comparing different strategies, the optimal treatment of SCAD is still controversial. The first-line approach is conservative and based on medical therapy. Nevertheless, in particular situations an invasive approach is necessary. In the last years, several new strategies have improved the way to perform percutaneous coronary interventions, such as new generation drug eluting stents, bio-resorbable scaffolds, sirolimus self-expandable stent, drug eluting balloons, and cutting balloon. Cardiac artery bypass graft is an even more invasive method to restore coronary flow and should be considered in urgent/emergent settings when PCI is not feasible or has failed.

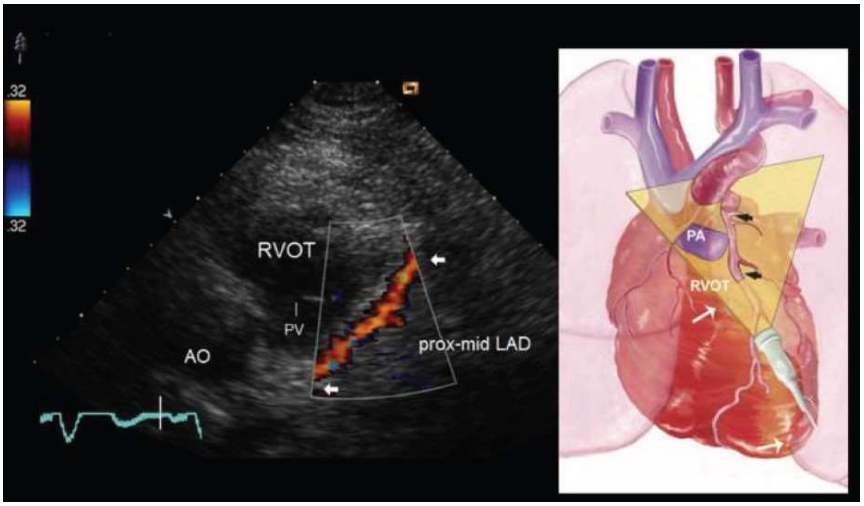
Cause the therapeutic approach of SCAD can be substantially different from that of atherosclerotic coronary artery disease, an accurate diagnosis is crucial to set up the best treatment strategy.

CHAPTER 12

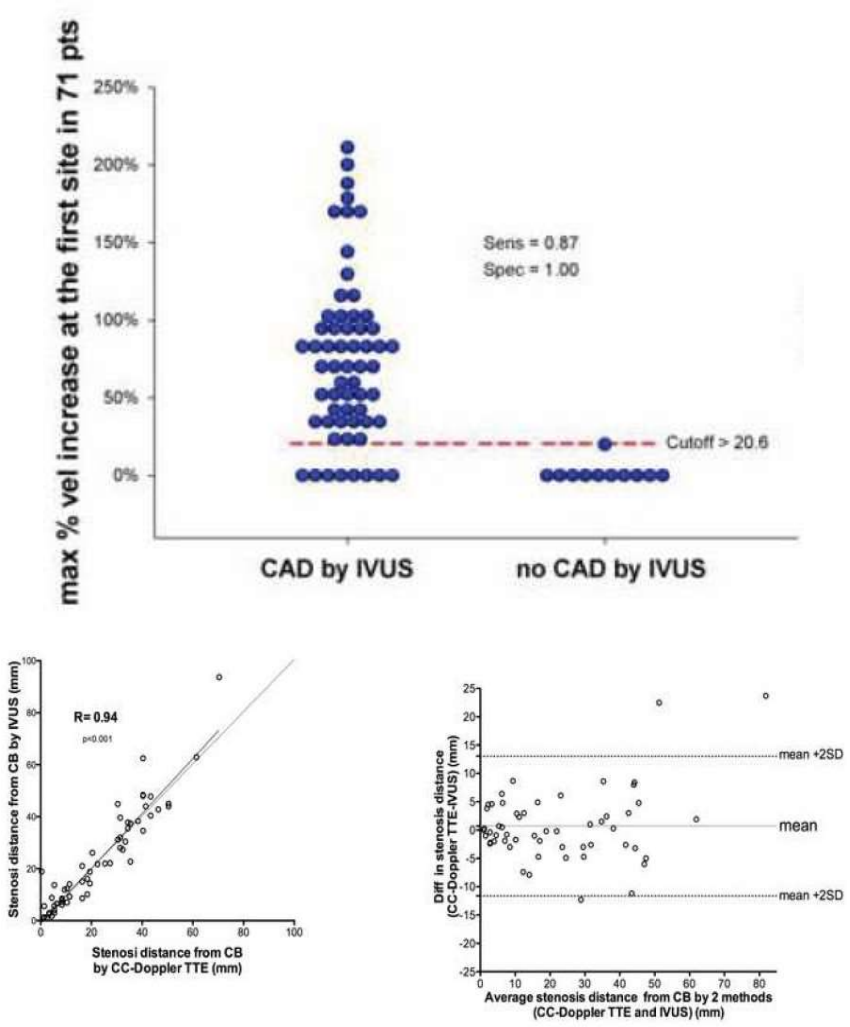
A new noninvasive method for assessing mild coronary coronary atherosclerosis: trans-thoracic convergent color Doppler after heart rate reduction. Validation versus intracoronary ultrasound

Background. A more sensitive transthoracic color Doppler technology (convergent color Doppler), along with a heart rate (HR) reduction and new tomographic planes, can greatly improve coronary blood flow velocity (BFV) recordings in the left main (LMCA) and left anterior descending (LAD) coronary arteries, allowing the detection of even a slight acceleration of BFV due to mild coronary stenosis.

Methods. A group of 26 patients underwent CC-Doppler-TTE in the LMCA and in the LAD coronary arteries before and after HR lowering. A second group of 71 patients scheduled for intravascular ultrasound underwent BFV Doppler recordings by CC-Doppler-TTE of the whole LAD (specifically the proximal, mid and distal segments) to detect a localized increase of BFV, after attaining maximal and reference BFV in each segment.



Results. In the first group, HR reduction dramatically improved the detection of optimal flow in the LMCA and LAD, from 4% to 54% and from 6% to 94% of the segments, respectively ($p < 0.001$). In the second group IVUS showed mild stenoses in 60 patients. Maximum velocity was higher in the diseased segment than normal segments (49 ± 24 vs 30 ± 9 cm/s; $p < 0.001$) and as the reference velocity was similar (32 ± 9 vs 30 ± 9cm/s; p = ns), the % increase was also higher ($52 \pm 52\%$ vs $0.5 \pm 3\%$; $p < 0.001$). Using a 22% increase in velocity as cut-off value, the sensitivity and specificity of CC-Doppler TTE in detecting at least one LAD plaque were 87% (52/60 pts) and 100% (11/11 pts), respectively. The lumen stenosis area (%), assessed by IVUS and by applying the CC-Doppler TTE continuity equation, was similar ($35 \pm 13\%$ vs $41 \pm 14\%$; $r = 0.55$; $p < 0.001$).



Conclusion. CC-Doppler-TTE evaluation of LAD BFV is greatly improved after reducing HR, allowing accurate non-invasive assessment of mild LAD stenosis with no radiation exposure.

CHAPTER 13

Establishing reference values for the diagnosis of coronary artery ectasia in current practice

INTRODUCTION

Coronary artery ectasia

Coronary artery ectasia (CAE), originally defined as a diffuse or segmental dilatation of the coronary artery with a diameter of more than 1.5 times the normal adjacent segments or the patient's largest coronary artery, was first described in 1976 by Markis et al [1]. Since then, the diagnosis of CAE has not evolved and it remains currently based on a comparative assessment of coronary diameters by visual estimation in reference to healthy vessels. This historical definition suffers from multiple limitations, including the impossibility to establish the diagnosis in patients with diffuse CAE as well as the lack of reproducibility derived from the absence of objective measures. Therefore, the inter-observer variability may play a significant role in the diagnosis and prevalence discrepancies reported by different investigators. So far, this has caused the true burden of CAE to be largely underestimated in fact the absence of reference values forces

interventional cardiologists to diagnose CAE only in the presence of self-evident and full-blown cases. Moreover, as stated above the current working definition impedes the diagnosis in patients with diffuse CAE in whom no reference artery diameter exists.

The reported prevalence varies between 0.2 and 10% in unselected series of patients referred for coronary artery angiography (CAG) with a reported 80% co-existence with obstructive coronary artery disease (CAD) [2]. The co-existence of CAE with coronary atherosclerosis raised the concept that ectasia may represent a variant of CAD [2-4] however a definite link between atherosclerosis and ectasia has not been confirmed.

Ectactic coronary arteries and the consequent impaired coronary blood flow is associated with complications including delayed antegrade coronary filling, segmental back flow phenomenon (milking phenomenon) and stasis in the dilated segments which can lead to ischemic heart disease, thrombus formation and possible distal embolization. Coronary artery aneurysm rupture is the most life-threatening complication which is associated with a significant rate of patient morbidity [5].

The clinical presentation of patients with CAE varies from asymptomatic to atypical chest pain, stable angina, acute coronary syndromes and sudden death. In those with a concomitant obstructive CAD, the symptoms are mostly believed to be associated with the severity of coexisting obstructive lesion. However, patients with isolated CAE may also present with stable angina, positive treadmill test, increased levels of biochemical markers or even myocardial infarction [6-7]. These observations suggest that CAE per se is a malignant condition, which can induce and be associated to myocardial ischemia and its related clinical consequences. At the same time, the appropriate diagnosis of CAE may help identifying these patients and support future studies on their optimal management. Indeed, there is no consensus regarding medical management of CAE (aspirin, P2Y12 inhibitors, and anticoagulants like warfarin have all been suggested but poorly investigated) and invasive management of these patients poses great challenges during percutaneous interventions due to large burden of thrombus, large diameters and high risk of vessel damage and rupture.

Normal coronary diameters

Only if the “normal” is defined we can truly determine the “abnormal”. Hence, the first step toward developing a more precise and practical definition for the CAE is to define the normal coronary artery diameters. Importantly, the same methodological approach has been followed for the thoracic or abdominal aorta reference diameters in order to establish the diagnosis of aneurismal conditions associated to its enlargement, whereas this rigorous scientific approach is currently missing for the coronary arteries.

In current available body of literature, the majority of studies with the aim of defining normal coronary artery diameters have been conducted during postmortem examinations of the heart [7]. The only two studies which focused on this subject by Vieweg et al. [8] and Dodge et al. [9] patients with valvular and structural heart disease were included, despite the fact that such conditions are known to influence the coronary lumen diameters by increased myocardial flow demand [10]. Dodge et al. demonstrated that the lumen diameter of most arterial sub-segments could be specified when gender, anatomic variation, branch length, and specific determinants of myocardial mass are taken into account. They indicated that in normal men, the combination of sub-segment location,

anatomic distribution pattern and the branch artery length categories provide an estimation of normal lumen diameter with a relatively small population variance [9]. However, it is noticeable that the above-mentioned studies were conducted years before the availability of the current advanced quantitative coronary measurement methods and as such they cannot form the basis for establishing the diagnosis of normal coronary arteries in current practice.

The continuously expanding implementation of CAG for investigation of cardiovascular disease warrants an undeniable need for standard reference measures to define the normal coronary artery luminal size and subsequently establish a diagnosis of CAE.

We have quantified the coronary artery luminal diameters in a rigorously selected normal healthy population in order to establish segment-specific, gender and body mass index normalized reference values for the coronary arteries. This will allow to develop reference thresholds for CAE diagnosis.

The proposed research project has major implications in the field of cardiology. It will form the basis for establishing the segment-specific reference coronary artery dimensions in normal and pathologic conditions.

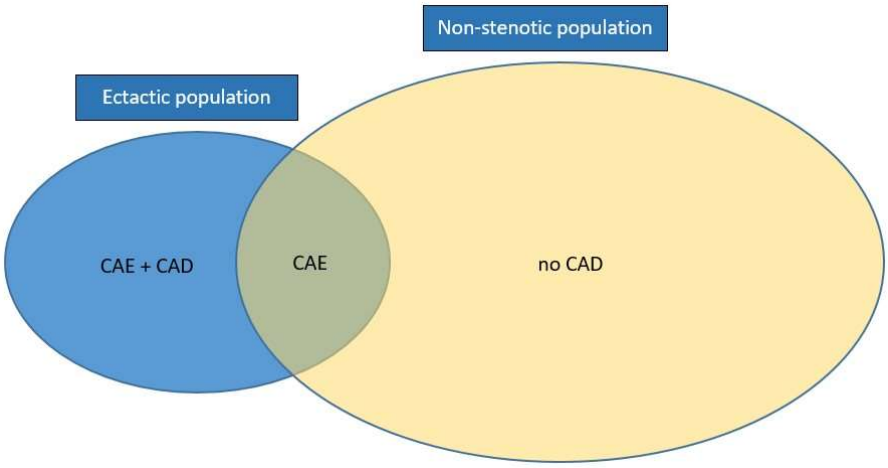
MATERIALS AND METHODS

Study population

Data of all consecutive patients between November 2014 and June 2018 who underwent CAG at Bern University Hospital and diagnosed with the terms “normal coronary arteries”, “coronary aneurysm”, “coronary ectasia” or “coronary dilation” in their catheterization reports have been retrospectively collected to generate the study database. Demographic features, medical comorbidities and therapy at the time of the CAG as well as during and after index hospitalization, data concerning cardiac clinical events occurring after discharge have been collected by the available medical reports and in form of a questionnaire.

Then a sequential two-step selection process based on the following inclusion and exclusion criteria have been applied. In the first step, the two populations of interest have been patients without any evidence of CAD (no quantified stenosis), labeled as the “*non-stenotic population*” (850 patients) and those with reported CAE, regardless of the presence or absence of concomitant CAD, which have been labeled as “*ectactic population*” (100 patients). In the second step, more stringent criteria to identify a normal coronary population have been employed to allocate

patients of the "non-stenotic population" into two the "*broad sample*" (727 subjects) and "*reference sample*" (123 subjects) categories. According to the further described inclusion and exclusion criteria, only 9 patients belong to both the ectactic population and the broad sample.



Inclusion and exclusion criteria

"Non-stenotic" and "ectactic" populations inclusion criteria are age ≥ 18 years; normal and/or ectatic coronary artery(ies); at least 4 available orthogonal angiographic projections of the left coronary artery and 2 orthogonal projections of right coronary artery; written informed consent (retrospectively collected) or waiver from the ethics committee. The exclusion criteria are: any evidence of CAD or prior self-limiting spontaneous coronary artery dissection; evidence of ischemia and/or

myocardial injury as assessed by high sensitivity troponin, valvular (at least of moderate severity), structural, congenital (including coronary anomalies, but excluding PFO, dextrocardia and situs viscerum inversus), infectious (endocarditis, myocarditis, pericarditis or combination of them) or neoplastic heart disease; left ventricular (LV) dysfunction; significant LV hypertrophy; evidence of any aortic lesions, such as atherosclerotic, aneurysm, dissection (acute or chronic), genetic, infectious, inflammatory or neoplastic aortic disease; evidence of intra-cardiac thrombosis; history of any interventional cardiovascular therapies; such as coronary revascularization, valvular repair or replacement and structural, aortic or peripheral arterial defects repair; prior heart, aortic and peripheral arteries surgery; admission due to congestive heart failure or cardiac arrest (in- or out-of-hospital); established or suspected peripheral arterial disease; connective tissue disease; brain death (potential organ donor) and pregnancy.

In order to further differentiate the “non-stenotic population” into its two sub-groups, criteria for “reference sample” are: no prior or intra-procedural administration of long-acting intravenous or intracoronary nitrates; no stroke or pulmonary embolism as the final diagnosis; absence of resistant or uncontrolled arterial hypertension, diabetes

mellitus, hypercholesterolemia, obesity or active smoking habit; no current or prior history of atrial fibrillation or any other cardiac arrhythmias; absence of aortic ectasia, isolated right ventricular failure or primary pulmonary hypertension; absence of acquired or congenital/syndromic peripheral arteriovenous malformations; stable hemodynamic conditions; absence of chronic lung, liver, kidney or thyroid dysfunction or being recipient of lung, liver or kidney transplantation; absence of anemia, thrombocytopenia or hemolytic failure; absence of known malignancy; absence of any autoimmune disease; absence of chronic or acute (last 2 months) infectious disease; no alcohol/drug abuse; no treatment with steroids; no recent (<3 months) surgery. The patients' medical history and physician-administered physical examination information, as well as data from biochemical and instrumental tests, such as EKG, transthoracic echocardiography or other imaging modalities if available have been obtained from the hospital's medical records. Blood pressure was routinely obtained during the catheterization admission in all cases.

Imaging analysis

Films have been inspected by two experienced interventional cardiologists. Depending on the vascularization of the inferior septum as well as inferior and posterior LV walls, four possible dominance patterns will be identified: right, “small” right, balanced and left. All segments and branches of the coronary artery tree have been identified, and the anatomy has been reduced to a set of up to 96 defined sub-segments (96 points in 32 defined coronary segments), according to Dodge et al [9]. In accordance to this methodology, terminal branches (diagonals, marginals, median ramus, etc.) have been classified by size into one of five groups: long, medium, short, absent, or unseen. This branch size rating refers to the vessel's length of distribution, not its width per se; where these vessels branched, their longest extension will be used.

Abbreviation	Name	Description
Main arteries		
LCA	Left coronary artery	
LM	Left main	
LAD	Left anterior descending	
LCx	Left circumflex	
RCA	Right coronary artery	
Main artery segments		

C1	LCx first segment	LCx from its origin at the LM to M1 (or OM, if M1 is absent)
C2	LCx second segment	LCx from Ml to M2 (or OM) (not present if Ml is absent)
C3	LCx third segment	LCx from M2 (or OM) to CP (if present, otherwise to end of LCx)
C4	LCx fourth segment	LCx from CP along atrioventricular groove to end of LCx (absent in RCA and small-RCA dominant distributions)
L1	LAD first segment	LAD from its origin at the LM to I septal branch (S1)
L2	LAD second segment	LAD from S1 to S3
L3	LAD third segment	LAD from S3 to the cardiac apex
L4	LAD fourth segment	LAD from the cardiac apex to its terminal point on the inferior wall
LM	Left main	LCA from ostium to bifurcation of LCA into LAD and LCx
R1	RCA first segment	RCA from its origin to I acute marginal branch (Al)
R2	RCA second segment	RCA from Al to A3
R3	RCA third segment	RCA from A3 to RD (if present, otherwise to end of RCA)
R4	RCA fourth segment	RCA from the RD along atrioventricular groove to end of RCA (absent in balanced and LCA dominant distributions)
Branch artery segments		
CD	Posterior descending	Distal most inferior wall branch arises from C4, present only in left-dominant anatomy
CI	Inferior	Inferior wall branch arises from C4 (present only in balanced and LCA dominant anatomy)

CP	Posterior	Proximal most inferior wall branch arises from junction of C3 and C4 (present in small-right, balanced, and LCA dominant anatomy)
D1-D3	Diagonals	Three largest branches arising from the LAD to supply the left ventricular anterior free wall, numbered from most proximal to most distal
M1-M3	Marginals	Three largest branches arising from the LCx to supply the left ventricular lateral free wall, numbered from most proximal to most distal
MR	Median ramus	An anatomic variant arising at a trifurcation of the LM
OA	Anterior branch OM	Anterior distal branch of OM
OM	Obtuse marginal	Anatomic variant present when one branch artery off the LCx is much larger than its neighbors supplying the left ventricular lateral free wall
OP	Posterior branch OM	Posterior distal branch of OM
RD	Posterior descending	Proximal most inferior wall branch arises from junction of R3 and R4 (present in right, small-right, and balanced dominant anatomy)
RI	Inferior	Inferior wall branch arises from R4 (present only in right and small-right dominant anatomy)
RP	Posterior	Distal most inferior wall branch arises from R4 (present only in right dominant anatomy)

The vessel diameters have been analyzed using a computerized bidimensional and tridimensional QCA analysis system (QAngio 7.3

and QAngio XA 3D, Medis medical imaging systems bv, Leiden, The Netherlands), which represents the latest technology available for QCA measures.

Statistical considerations

When data are neither gaussian or log-gaussian, and/or an incorrect distribution of the data is assumed, nonparametric estimates are preferable and more reliable. When neither assumption is true, nonparametric estimates hold. Among the several nonparametric estimates, with the aim to determine the normal range based on the QCA images of the "non-stenotic population", we have employed the percentile estimates together with nonparametric confidence intervals for the true percentile. The least sample size, which permits 90% confidence intervals for the normal limits, is 120 subjects. On this basis, n = 120 is the minimum number of samples needed for the reference sample to calculate normal range estimates. Utilizing this method, we have classified values of each angiographic variable into the following five categories based on sex- and BMI-specific percentiles (indicating increasing deviation from the reference limits): category 0 (reference limits): value $\leq 95^{th}$ percentile of the reference sample; category 1

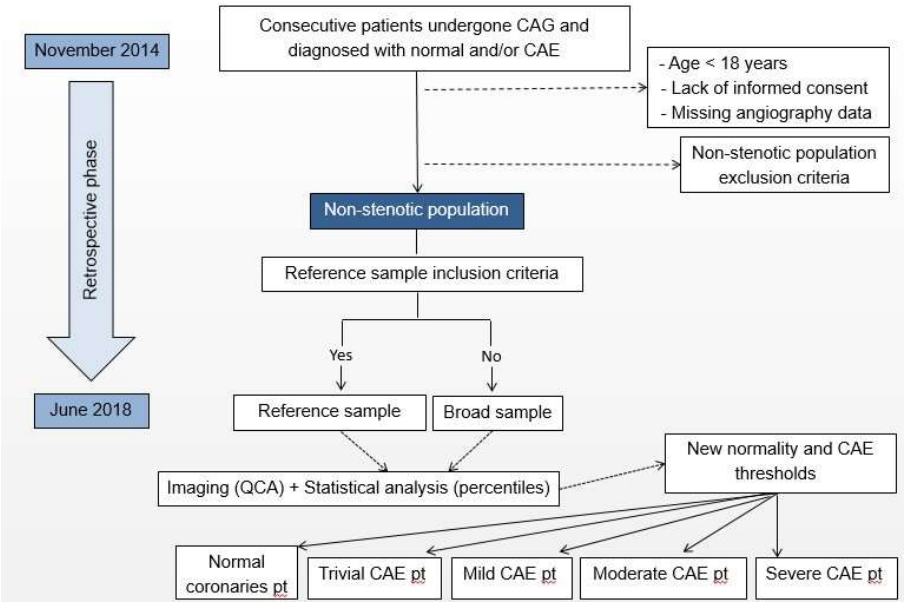
(trivial CAE): 95th percentile of reference sample < value ≤ 95th percentile of broad sample; category 2 (mild CAE): 95th percentile of broad sample < value ≤ 98th percentile of broad sample; category 3 (moderate CAE): 98th percentile of broad sample < value ≤ 99th percentile of broad sample; category 4 (severe CAE): value > 99th percentile of broad sample

Statistical analyses have been performed with SPSS version 25.0 and Stata 14.0. Continuous variables have been summarized as mean ± standard deviation or median ± 95% confidence interval, depending on normality of distribution. Categorical variables have been expressed as frequencies and percentages. Comparisons between continuous data have been performed using unpaired t-test and Wilcoxon test (or Mann–Whitney U test when appropriate), depending on normality of distribution. Normality will be assessed using Kolmogorow-Smirnow test. Comparisons between categorical data heve been performed using Chi-squares test (or Fisher exact test when appropriate). Statistical significance threshold has been set at a p-value <0.05.

Good Clinical Practice (GCP) Statement

This study has been conducted in accordance with the protocol, the Declaration of Helsinki, the principles of Good Clinical Practice (GCP), the Human Research Act (HRA) and the Human Research Ordinance (HRO) as well as other locally relevant regulations.

Flowchart of the study



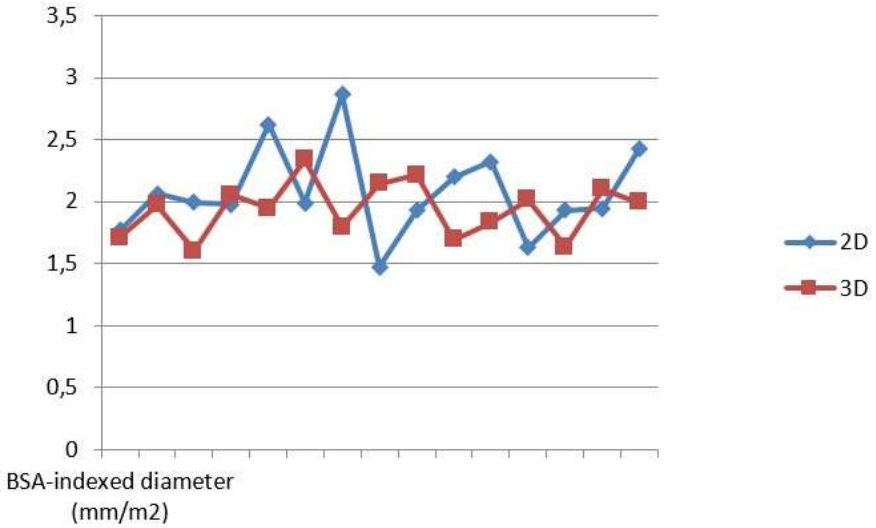
PRELIMINARY RESULTS

Reference sample: segments length comparison between 2D and 3D evaluation.

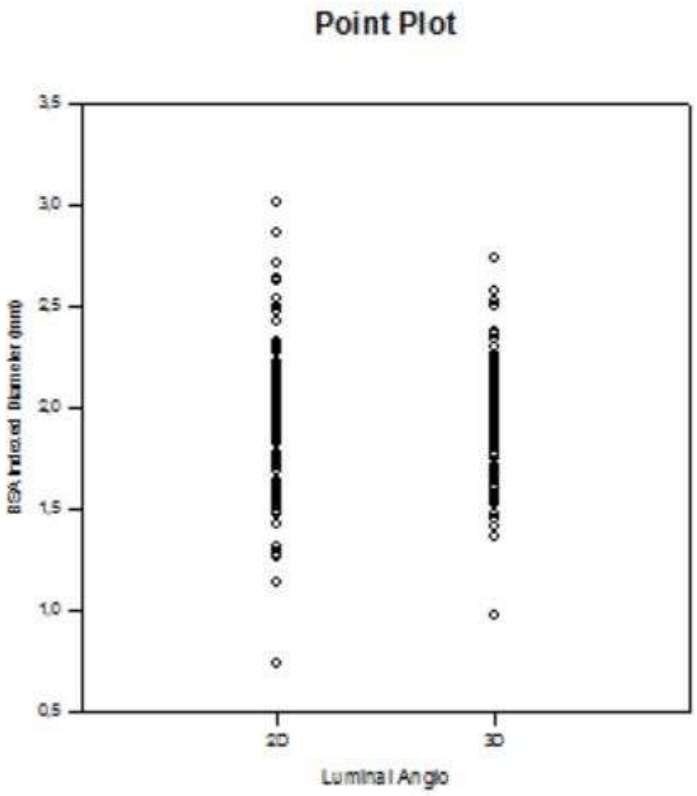
Segments	n	2D mean (SD) (mm)	n	3D mean (SD) (mm)	p (paired t-test)
LM	113	9.66 (3.84)	96	11.8 (4.62)	7,98E-10
L1	123	22.4 (9.35)	116	24.5 (11.3)	0,00338
L2	123	37.4 (12.5)	115	40.8 (13.9)	2,63E-07
L3	122	59.8 (12.9)	111	69.5 (14.3)	8,39E-18
L4	95	29.7 (11.4)	64	33.4 (11.4)	0,00153
D1	112	55.9 (21.8)	68	65.9 (25.2)	6,74E-05
D2	85	44.8 (19.5)	59	52.7 (23.2)	1,14E-05
D3	34	31.6 (14.7)	21	36.2 (18.3)	0,233
MR	52	59.6 (23.2)	40	72.7 (29)	0,00278
C1	123	20.4 (12.5)	117	22.9 (13.1)	7,66E-10
C2	115	24.1 (11.8)	104	29.1 (14)	2,14E-10
C3	88	24.7 (11.9)	68	26.8 (13.8)	0,00945
C4	31	18.9 (12.4)	17	23.1 (14)	0,0655
OM	79	48.7 (28)	75	55.7 (32.8)	0,000521
OA	42	50.3 (22.5)	36	52.2 (18.9)	0,0663
OP	42	45 (21.8)	37	49.5 (19.2)	0,00191
M1	63	48 (21.6)	36	61.7 (18.6)	0,0169
M2	72	39.6 (20.1)	41	47 (23.3)	0,0988
M3	28	37 (21.4)	17	49.1 (24.7)	0,0536
CP	53	40.7 (20.5)	33	44.3 (18.3)	0,387
CI	31	32.7 (16.4)	14	38.3 (21.3)	0,306
CD	9	38.3 (11.3)	3	36.8 (5.98)	0,655
R1	123	25.7 (10.8)	104	28.1 (11.1)	0,000594

R2	123	29.1 (11.3)	104	31.6 (12.8)	1,53E-06
R3	122	43.5 (15.4)	93	49.3 (16.2)	3,51E-08
R4	92	32.9 (18.1)	60	36 (18.9)	0,0436
RD	114	57.9 (18.5)	64	63.1 (16.8)	0,000404
RI	92	41.4 (19.5)	33	42.8 (16.9)	0,819
RP	69	47.1 (23)	27	52 (26.2)	0,477

Reference sample: scatterplot showing BSA-indexed L1 (proximal LAD) diameters variation according to 2D (n = 123) or 3D (n = 116) evaluation.



Reference sample: point plot showing BSA-indexed L1 (proximal LAD) diameters variation according to 2D or 3D evaluation; p = 0,197.



Reference sample: variations of main segments 2D non-indexed diameters according to Dodge dominance in males.

Main segments	right		small right		balanced		left		p
	n	mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)	
LM	34	4.38 (0.724)	9	4.41 (0.759)	10	5.35 (0.71)	5	4.61 (0.658)	0.0112
L1	35	3.64 (0.77)	12	3.91 (0.583)	11	4.06 (0.468)	6	3.68 (0.491)	0.177
L2	35	2.81 (0.549)	12	3.11 (0.509)	11	2.96 (0.28)	6	2.85 (0.436)	0.296

L3	35	1.92 (0.429)	12	2.16 (0.398)	11	2.22 (0.343)	6	2.25 (0.463)	0.0715
L4	27	1.24 (0.414)	9	1.38 (0.354)	10	1.33 (0.141)	6	1.55 (0.265)	0.166
C1	35	3.07 (0.753)	12	3.63 (0.408)	11	4.35 (0.951)	6	3.84 (0.66)	0.000103
C2	31	2.23 (0.761)	12	2.84 (0.82)	11	3.29 (0.66)	6	3.35 (0.686)	0.000431
C3	16	1.4 (0.491)	12	1.99 (0.415)	11	2.7 (0.805)	6	2.45 (0.37)	1.51e-05
C4	0	NaN (NA)	0	NaN (NA)	11	2.01 (0.65)	6	1.89 (0.412)	NaN
R1	35	4.14 (0.685)	12	4.06 (0.268)	11	3.64 (0.697)	6	2.88 (0.269)	0.000373
R2	35	3.96 (0.683)	12	3.76 (0.321)	11	3.01 (0.822)	6	2.13 (0.411)	3.04e-05
R3	35	3.49 (0.561)	12	3.24 (0.446)	10	2.51 (0.815)	6	1.25 (0.311)	1.18e-05
R4	35	2.49 (0.469)	12	2.2 (0.404)	0	NaN (NA)	0	NaN (NA)	NaN

Reference sample: variations of main segments 2D non-indexed diameters according to Dodge dominance in females.

Main segments	right		small right		balanced		left		p
	n	mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)	
LM	33	4.04 (0.648)	10	3.88 (0.437)	10	4.05 (0.389)	2	4.51 (0.676)	0.547
L1	34	3.59 (0.565)	11	3.16 (0.591)	11	3.22 (0.607)	3	2.94 (0.515)	0.0407
L2	34	2.71 (0.579)	11	2.36 (0.423)	11	2.48 (0.64)	3	2.35 (0.0337)	0.216
L3	34	1.69 (0.38)	10	1.63 (0.362)	11	1.69 (0.509)	3	1.9 (0.13)	0.722
L4	23	1.15 (0.26)	8	1.08 (0.259)	9	1.12 (0.241)	3	1.18 (0.153)	0.794
C1	34	2.97 (0.62)	11	2.76 (0.43)	11	3.36 (0.814)	3	3.67 (0.326)	0.0358

C2	31	2.13 (0.765)	10	2.22 (0.537)	11	2.84 (0.493)	3	3.11 (0.206)	0.00711
C3	19	1.46 (0.741)	10	1.54 (0.382)	11	2.39 (0.514)	3	2.6 (0.18)	0.000422
C4	0	NaN (NA)	0	NaN (NA)	11	1.75 (0.461)	3	2.06 (0.175)	NaN
R1	34	3.71 (0.563)	11	3.4 (0.46)	11	3.08 (0.386)	3	2.25 (0.241)	0.000266
R2	34	3.54 (0.658)	11	3.09 (0.422)	11	2.78 (0.403)	3	1.93 (0.164)	0.00011
R3	34	3.21 (0.63)	11	2.74 (0.304)	11	2.26 (0.477)	3	1.27 (0.128)	4.98e-06
R4	34	2.41 (0.558)	11	1.63 (0.34)	0	NaN (NA)	0	NaN (NA)	NaN

Reference sample: variations of main segments 3D non-indexed diameters according to Dodge dominance in males.

Main segments	right		small right		balanced		left		p
	n	mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)	
LM	29	4.2 (0.636)	8	4.19 (0.715)	7	4.77 (0.649)	4	4.69 (0.528)	0.144
L1	33	3.55 (0.623)	11	3.69 (0.518)	11	3.8 (0.525)	6	3.58 (0.372)	0.588
L2	31	2.71 (0.338)	11	2.97 (0.454)	11	2.83 (0.257)	6	2.78 (0.357)	0.239
L3	32	1.84 (0.339)	10	2.2 (0.429)	9	2.1 (0.273)	5	2.18 (0.416)	0.0529
L4	17	1.19 (0.282)	6	1.41 (0.333)	5	1.32 (0.186)	4	1.38 (0.262)	0.39
C1	32	2.85 (0.592)	11	3.48 (0.433)	10	4 (0.697)	6	3.82 (0.651)	2.48e-05
C2	25	2.22 (0.543)	11	2.66 (0.822)	10	3.07 (0.395)	6	3.21 (0.754)	0.000364
C3	11	1.46 (0.469)	9	1.84 (0.509)	10	2.31 (0.661)	5	2.53 (0.624)	0.00309
C4	0	NaN (NA)	0	NaN (NA)	6	1.98 (0.663)	3	2 (0.264)	NaN

R1	29	4.05 (0.599)	11	3.95 (0.381)	11	3.38 (0.511)	5	2.68 (0.249)	0.000127
R2	30	3.78 (0.544)	10	3.6 (0.485)	10	2.89 (0.636)	5	1.94 (0.281)	3.24e-05
R3	26	3.22 (0.465)	10	3.01 (0.327)	9	2.34 (0.618)	5	1.15 (0.189)	1.4e-05
R4	25	2.29 (0.444)	8	1.95 (0.445)	0	NaN (NA)	0	NaN (NA)	NaN

Reference sample: variations of main segments 3D non-indexed diameters according to Dodge dominance in females.

Main segments	right		small right		balanced		left		p
	n	mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)	
LM	28	3.94 (0.417)	9	3.86 (0.424)	10	4.16 (0.358)	1	3.96 (NA)	0.457
L1	33	3.43 (0.425)	9	3.18 (0.518)	10	3.33 (0.256)	3	2.94 (0.553)	0.252
L2	34	2.58 (0.454)	9	2.37 (0.36)	10	2.57 (0.327)	3	2.23 (0.0876)	0.268
L3	33	1.65 (0.342)	9	1.64 (0.269)	10	1.78 (0.24)	3	1.8 (0.147)	0.512
L4	18	1.09 (0.255)	6	1.17 (0.287)	7	1.13 (0.144)	1	1.18 (NA)	0.943
C1	34	2.9 (0.496)	10	2.73 (0.469)	11	3.33 (0.568)	3	3.72 (0.176)	0.00716
C2	29	2.07 (0.624)	10	2.19 (0.543)	10	2.75 (0.394)	3	3.01 (0.331)	0.00465
C3	13	1.48 (0.573)	8	1.46 (0.337)	9	2.4 (0.432)	3	2.46 (0.0626)	0.000929
C4	0	NaN (NA)	0	NaN (NA)	7	1.85 (0.401)	1	2.21 (NA)	NaN
R1	28	3.56 (0.535)	10	3.26 (0.443)	9	3.14 (0.283)	1	2.1 (NA)	0.0288
R2	28	3.36 (0.6)	10	2.96 (0.375)	10	2.81 (0.384)	1	2.03 (NA)	0.013
R3	25	3.04 (0.569)	8	2.59 (0.311)	9	2.23 (0.439)	1	1.23 (NA)	0.000309

R4	22	2.23 (0.512)	5	1.62 (0.367)	0	NaN (NA)	0	NaN (NA)	NaN

Reference sample: variations of main segments 2D BSA-indexed diameters according to Dodge dominance in males.

Main segments	right		small right		balanced		left		p
	n	mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)	
LM	34	2.24 (0.322)	9	2.07 (0.332)	10	2.62 (0.46)	5	2.37 (0.396)	0.0478
L1	35	1.86 (0.374)	12	1.9 (0.317)	11	1.99 (0.274)	6	1.85 (0.169)	0.588
L2	35	1.43 (0.24)	12	1.5 (0.232)	11	1.45 (0.154)	6	1.43 (0.163)	0.783
L3	35	0.981 (0.2)	12	1.04 (0.162)	11	1.09 (0.183)	6	1.13 (0.176)	0.226
L4	27	0.632 (0.193)	9	0.665 (0.14)	10	0.65 (0.0941)	6	0.778 (0.0921)	0.123
C1	35	1.56 (0.343)	12	1.76 (0.177)	11	2.15 (0.584)	6	1.94 (0.313)	0.000536
C2	31	1.13 (0.372)	12	1.38 (0.387)	11	1.62 (0.368)	6	1.69 (0.314)	0.000917
C3	16	0.707 (0.253)	12	0.968 (0.234)	11	1.33 (0.466)	6	1.23 (0.134)	5.53e-05
C4	0	NaN (NA)	0	NaN (NA)	11	0.995 (0.384)	6	0.95 (0.167)	NaN
R1	35	2.12 (0.35)	12	1.97 (0.211)	11	1.78 (0.32)	6	1.45 (0.0987)	4.92e-05
R2	35	2.03 (0.372)	12	1.82 (0.177)	11	1.46 (0.358)	6	1.08 (0.197)	4.15e-06
R3	35	1.79 (0.306)	12	1.57 (0.196)	10	1.23 (0.378)	6	0.632 (0.164)	1.76e-06
R4	35	1.28 (0.251)	12	1.06 (0.17)	0	NaN (NA)	0	NaN (NA)	NaN

Reference sample: variations of main segments 2D BSA-indexed diameters according to Dodge dominance in females.

Main segments	right		small right		balanced		left		p
	n	mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)	
LM	33	2.37 (0.399)	10	2.28 (0.327)	10	2.43 (0.257)	2	2.7 (0.488)	0.562
L1	34	2.1 (0.35)	11	1.87 (0.351)	11	1.92 (0.345)	3	1.8 (0.302)	0.134
L2	34	1.59 (0.365)	11	1.39 (0.231)	11	1.48 (0.365)	3	1.44 (0.0791)	0.402
L3	34	0.987 (0.219)	10	0.958 (0.199)	11	1.01 (0.29)	3	1.17 (0.0742)	0.371
L4	23	0.661 (0.131)	8	0.635 (0.174)	9	0.665 (0.121)	3	0.719 (0.0595)	0.733
C1	34	1.74 (0.375)	11	1.62 (0.177)	11	1.98 (0.387)	3	2.26 (0.296)	0.0145
C2	31	1.25 (0.463)	10	1.3 (0.277)	11	1.69 (0.265)	3	1.91 (0.103)	0.00125
C3	19	0.865 (0.467)	10	0.906 (0.212)	11	1.42 (0.289)	3	1.6 (0.185)	0.000307
C4	0	NaN (NA)	0	NaN (NA)	11	1.04 (0.249)	3	1.26 (0.102)	NaN
R1	34	2.17 (0.342)	11	2.01 (0.289)	11	1.83 (0.207)	3	1.38 (0.172)	0.000681
R2	34	2.07 (0.396)	11	1.82 (0.247)	11	1.66 (0.25)	3	1.19 (0.147)	0.000321
R3	34	1.88 (0.368)	11	1.62 (0.154)	11	1.35 (0.265)	3	0.784 (0.117)	1.14e-05
R4	34	1.42 (0.37)	11	0.962 (0.199)	0	NaN (NA)	0	NaN (NA)	

Reference sample: variations of main segments 3D BSA-indexed diameters according to Dodge dominance in males.

Main segments	right		small right		balanced		left		p
	n	mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)	
LM	29	2.16 (0.359)	8	1.95 (0.27)	7	2.32 (0.415)	4	2.44 (0.345)	0.147
L1	33	1.83 (0.335)	11	1.78 (0.262)	11	1.86 (0.302)	6	1.81 (0.155)	0.912
L2	31	1.4 (0.196)	11	1.43 (0.174)	11	1.39 (0.182)	6	1.4 (0.157)	0.867
L3	32	0.947 (0.184)	10	1.06 (0.175)	9	1.04 (0.161)	5	1.11 (0.166)	0.134
L4	17	0.612 (0.131)	6	0.668 (0.129)	5	0.658 (0.138)	4	0.694 (0.0874)	0.598
C1	32	1.47 (0.294)	11	1.68 (0.192)	10	1.98 (0.432)	6	1.93 (0.312)	0.000748
C2	25	1.14 (0.291)	11	1.28 (0.377)	10	1.52 (0.241)	6	1.62 (0.348)	0.00165
C3	11	0.756 (0.242)	9	0.906 (0.268)	10	1.14 (0.384)	5	1.26 (0.272)	0.00687
C4	0	NaN (NA)	0	NaN (NA)	6	0.996 (0.406)	3	0.987 (0.13)	NaN
R1	29	2.08 (0.336)	11	1.9 (0.201)	11	1.65 (0.204)	5	1.37 (0.123)	1.05e-05
R2	30	1.94 (0.349)	10	1.72 (0.195)	10	1.4 (0.261)	5	1 (0.177)	3.34e-06
R3	26	1.63 (0.229)	10	1.44 (0.139)	9	1.13 (0.266)	5	0.595 (0.127)	2.34e-06
R4	25	1.17 (0.233)	8	0.938 (0.145)	0	NaN (NA)	0	NaN (NA)	NaN

Reference sample: variations of main segments 3D BSA-indexed diameters according to Dodge dominance in females.

Main segments	right		small right		balanced		left		p
	n	mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)	
LM	28	2.29 (0.278)	9	2.25 (0.271)	10	2.51 (0.348)	1	2.31 (NA)	0.254
L1	33	2 (0.248)	9	1.88 (0.306)	10	2 (0.217)	3	1.8 (0.342)	0.376
L2	34	1.51 (0.278)	9	1.42 (0.21)	10	1.54 (0.24)	3	1.37 (0.0947)	0.663
L3	33	0.964 (0.183)	9	0.986 (0.164)	10	1.07 (0.163)	3	1.11 (0.136)	0.247
L4	18	0.633 (0.13)	6	0.708 (0.194)	7	0.701 (0.0844)	1	0.759 (NA)	0.577
C1	34	1.7 (0.31)	10	1.61 (0.238)	11	1.98 (0.281)	3	2.28 (0.147)	0.0011
C2	29	1.21 (0.377)	10	1.28 (0.269)	10	1.64 (0.232)	3	1.84 (0.159)	0.00132
C3	13	0.869 (0.366)	8	0.856 (0.198)	9	1.42 (0.29)	3	1.51 (0.076)	0.00144
C4	0	NaN (NA)	0	NaN (NA)	7	1.08 (0.231)	1	1.35 (NA)	NaN
R1	28	2.07 (0.333)	10	1.92 (0.244)	9	1.87 (0.249)	1	1.35 (NA)	0.0733
R2	28	1.96 (0.363)	10	1.74 (0.186)	10	1.69 (0.305)	1	1.31 (NA)	0.135
R3	25	1.77 (0.335)	8	1.51 (0.124)	9	1.31 (0.283)	1	0.793 (NA)	0.00136
R4	22	1.31 (0.338)	5	0.914 (0.222)	0	NaN (NA)	0	NaN (NA)	NaN

Reference sample: variations of main segments 2D height-indexed diameters according to Dodge dominance in males.

Main segments	right		small right		balanced		left		p
	n	mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)	
LM	34	2.47 (0.396)	9	2.41 (0.376)	10	2.97 (0.446)	5	2.63 (0.36)	0.0135
L1	35	2.05 (0.413)	12	2.17 (0.323)	11	2.25 (0.274)	6	2.07 (0.226)	0.322
L2	35	1.58 (0.298)	12	1.72 (0.251)	11	1.64 (0.163)	6	1.61 (0.216)	0.387
L3	35	1.08 (0.236)	12	1.19 (0.19)	11	1.23 (0.196)	6	1.27 (0.238)	0.0761
L4	27	0.699 (0.232)	9	0.762 (0.169)	10	0.737 (0.0869)	6	0.875 (0.133)	0.13
C1	35	1.73 (0.412)	12	2.01 (0.208)	11	2.42 (0.589)	6	2.17 (0.331)	0.000143
C2	31	1.25 (0.428)	12	1.58 (0.45)	11	1.83 (0.392)	6	1.89 (0.359)	0.000496
C3	16	0.785 (0.29)	12	1.1 (0.242)	11	1.5 (0.484)	6	1.38 (0.166)	3.66e-05
C4	0	NaN (NA)	0	NaN (NA)	11	1.12 (0.395)	6	1.07 (0.207)	NaN
R1	35	2.33 (0.36)	12	2.25 (0.152)	11	2.02 (0.38)	6	1.63 (0.127)	0.000159
R2	35	2.23 (0.383)	12	2.08 (0.166)	11	1.66 (0.444)	6	1.21 (0.221)	1.42e-05
R3	35	1.97 (0.306)	12	1.79 (0.219)	10	1.39 (0.441)	6	0.708 (0.185)	5.59e-06
R4	35	1.4 (0.26)	12	1.21 (0.203)	0	NaN (NA)	0	NaN (NA)	NaN

Reference sample: variations of main segments 2D height-indexed diameters according to Dodge dominance in females.

Main segments	right		small right		balanced		left		p
	n	mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)	
LM	33	2.46 (0.386)	10	2.34 (0.287)	10	2.45 (0.245)	2	2.8 (0.395)	0.479
L1	34	2.18 (0.342)	11	1.91 (0.348)	11	1.95 (0.377)	3	1.83 (0.307)	0.0488
L2	34	1.65 (0.355)	11	1.43 (0.24)	11	1.5 (0.386)	3	1.46 (0.0118)	0.216
L3	34	1.03 (0.227)	10	0.985 (0.209)	11	1.02 (0.302)	3	1.18 (0.0729)	0.444
L4	23	0.692 (0.153)	8	0.651 (0.164)	9	0.677 (0.141)	3	0.732 (0.097)	0.721
C1	34	1.8 (0.376)	11	1.66 (0.223)	11	2.03 (0.485)	3	2.29 (0.196)	0.0307
C2	31	1.3 (0.48)	10	1.34 (0.291)	11	1.72 (0.288)	3	1.94 (0.139)	0.00332
C3	19	0.895 (0.489)	10	0.929 (0.216)	11	1.45 (0.321)	3	1.62 (0.119)	0.000373
C4	0	NaN (NA)	0	NaN (NA)	11	1.06 (0.283)	3	1.28 (0.0996)	NaN
R1	34	2.25 (0.332)	11	2.06 (0.269)	11	1.87 (0.245)	3	1.4 (0.159)	0.000114
R2	34	2.15 (0.392)	11	1.86 (0.233)	11	1.68 (0.254)	3	1.2 (0.109)	4.57e-05
R3	34	1.95 (0.371)	11	1.66 (0.164)	11	1.37 (0.284)	3	0.794 (0.0823)	2.78e-06
R4	34	1.47 (0.35)	11	0.985 (0.207)	0	NaN (NA)	0	NaN (NA)	NaN

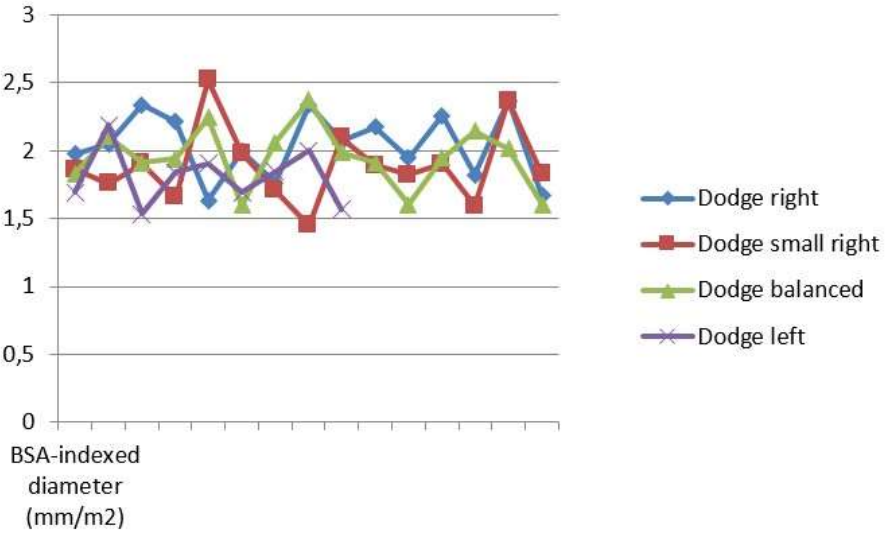
Reference sample: variations of main segments 3D height-indexed diameters according to Dodge dominance in males.

Main segments	right		small right		balanced		left		p
	n	mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)	
LM	29	2.37 (0.355)	8	2.27 (0.332)	7	2.63 (0.373)	4	2.7 (0.323)	0.118
L1	33	2 (0.341)	11	2.04 (0.263)	11	2.11 (0.305)	6	2.02 (0.153)	0.835
L2	31	1.53 (0.197)	11	1.63 (0.201)	11	1.57 (0.165)	6	1.57 (0.174)	0.394
L3	32	1.04 (0.198)	10	1.21 (0.21)	9	1.17 (0.162)	5	1.24 (0.231)	0.0767
L4	17	0.674 (0.16)	6	0.773 (0.155)	5	0.736 (0.121)	4	0.777 (0.13)	0.403
C1	32	1.61 (0.322)	11	1.92 (0.213)	10	2.23 (0.422)	6	2.16 (0.327)	6.37e-05
C2	25	1.25 (0.314)	11	1.47 (0.441)	10	1.71 (0.238)	6	1.81 (0.396)	0.000887
C3	11	0.834 (0.283)	9	1.02 (0.284)	10	1.28 (0.396)	5	1.43 (0.314)	0.00346
C4	0	NaN (NA)	0	NaN (NA)	6	1.11 (0.41)	3	1.13 (0.128)	NaN
R1	29	2.28 (0.326)	11	2.18 (0.187)	11	1.87 (0.271)	5	1.52 (0.126)	6.22e-05
R2	30	2.13 (0.33)	10	1.98 (0.229)	10	1.6 (0.339)	5	1.11 (0.182)	1.45e-05
R3	26	1.81 (0.252)	10	1.66 (0.16)	9	1.29 (0.326)	5	0.66 (0.131)	4.01e-06
R4	25	1.29 (0.243)	8	1.07 (0.204)	0	NaN (NA)	0	NaN (NA)	NaN

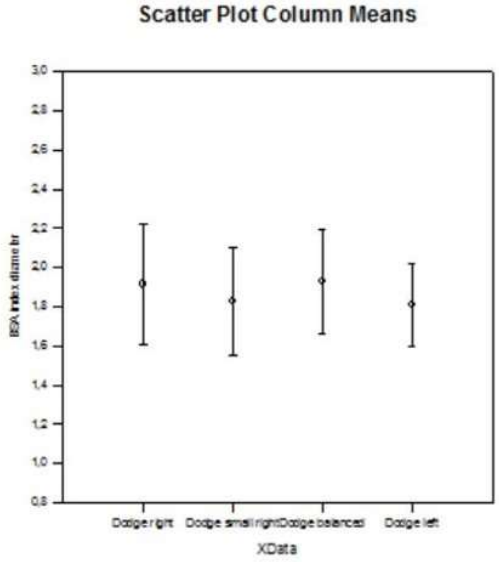
Reference sample: variations of main segments 3D height-indexed diameters according to Dodge dominance in females.

Main segments	right		small right		balanced		left		p
	n	mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)	
LM	28	2.39 (0.246)	9	2.31 (0.266)	10	2.52 (0.237)	1	2.47 (NA)	0.402
L1	33	2.08 (0.238)	9	1.93 (0.298)	10	2.03 (0.187)	3	1.83 (0.33)	0.209
L2	34	1.57 (0.263)	9	1.45 (0.211)	10	1.56 (0.205)	3	1.39 (0.045)	0.402
L3	33	1 (0.193)	9	1 (0.164)	10	1.09 (0.14)	3	1.12 (0.0878)	0.379
L4	18	0.656 (0.146)	6	0.717 (0.186)	7	0.694 (0.0895)	1	0.735 (NA)	0.816
C1	34	1.76 (0.293)	10	1.65 (0.265)	11	2.01 (0.338)	3	2.32 (0.0924)	0.00413
C2	29	1.26 (0.386)	10	1.32 (0.29)	10	1.67 (0.242)	3	1.87 (0.216)	0.00228
C3	13	0.904 (0.388)	8	0.882 (0.191)	9	1.45 (0.294)	3	1.53 (0.0279)	0.00109
C4	0	NaN (NA)	0	NaN (NA)	7	1.13 (0.249)	1	1.37 (NA)	NaN
R1	28	2.16 (0.299)	10	1.97 (0.246)	9	1.91 (0.211)	1	1.31 (NA)	0.0233
R2	28	2.04 (0.341)	10	1.79 (0.189)	10	1.71 (0.259)	1	1.27 (NA)	0.023
R3	25	1.84 (0.324)	8	1.56 (0.162)	9	1.36 (0.276)	1	0.769 (NA)	0.000212
R4	22	1.35 (0.307)	5	0.968 (0.238)	0	NaN (NA)	0	NaN (NA)	NaN

Reference sample: scatterplot showing BSA-indexed L1 (proximal LAD) 3D diameters variation according to Dodge dominances: right dominance (n = 66), small right dominance (n = 20), balanced dominance (n = 21), left dominance (n = 9).



Reference sample: scatterplot showing BSA-indexed L1 (proximal LAD) 3D diameters variation according to Dodge dominances; p = 0,484.



Reference sample: variations of main segments non-indexed diameters according to Syntax dominance in males.

	2D				p	3D				p
	right		left			right		left		
	n	mean (SD)	n	mean (SD)		n	mean (SD)	n	mean (SD)	
LM	53	4.57 (0.807)	5	4.61 (0.658)	0.9	44	4.29 (0.671)	4	4.69 (0.528)	0.235
L1	58	3.78 (0.698)	6	3.68 (0.491)	0.662	55	3.63 (0.584)	6	3.58 (0.372)	0.807
L2	58	2.9 (0.508)	6	2.85 (0.436)	0.772	53	2.79 (0.359)	6	2.78 (0.357)	0.931
L3	58	2.03 (0.423)	6	2.25 (0.463)	0.307	51	1.96 (0.375)	5	2.18 (0.416)	0.301
L4	46	1.29 (0.359)	6	1.55 (0.265)	0.0621	28	1.26 (0.286)	4	1.38 (0.262)	0.44
C1	58	3.43 (0.885)	6	3.84 (0.66)	0.203	53	3.2 (0.74)	6	3.82 (0.651)	0.0677
C2	54	2.58 (0.862)	6	3.35 (0.686)	0.0389	46	2.51 (0.68)	6	3.21 (0.754)	0.0716
C3	39	1.95 (0.778)	6	2.45 (0.37)	0.0222	30	1.86 (0.642)	5	2.53 (0.624)	0.0726
C4	11	2.01 (0.65)	6	1.89 (0.412)	0.663	6	1.98 (0.663)	3	2 (0.264)	0.926
R1	58	4.03 (0.644)	6	2.88 (0.269)	2.19e-06	51	3.88 (0.595)	5	2.68 (0.249)	8.02e-06
R2	58	3.74 (0.74)	6	2.13 (0.411)	1.93e-05	50	3.56 (0.643)	5	1.94 (0.281)	2.32e-06
R3	57	3.27 (0.687)	6	1.25 (0.311)	4.57e-08	45	2.99 (0.576)	5	1.15 (0.189)	1.5e-10

Reference sample: variations of main segments non-indexed diameters according to Syntax dominance in females.

	2D				p	3D				p
	right		left			right		left		
	n	mean (SD)	n	mean (SD)		n	mean (SD)	n	mean (SD)	
LM	53	4.01 (0.567)	2	4.51 (0.676)		47	3.97 (0.411)	1	3.96 (NA)	

L1	56	3.44 (0.601)	3	2.94 (0.515)	0.229	52	3.37 (0.419)	3	2.94 (0.553)	0.313
L2	56	2.6 (0.574)	3	2.35 (0.0337)	0.00324	53	2.54 (0.419)	3	2.23 (0.0876)	0.00239
L3	55	1.68 (0.398)	3	1.9 (0.13)	0.0642	52	1.67 (0.313)	3	1.8 (0.147)	0.268
L4	40	1.13 (0.251)	3	1.18 (0.153)	0.634	31	1.11 (0.236)	1	1.18 (NA)	
C1	56	3.01 (0.651)	3	3.67 (0.326)	0.0497	55	2.95 (0.536)	3	3.72 (0.176)	0.00239
C2	52	2.3 (0.724)	3	3.11 (0.206)	0.00228	49	2.23 (0.621)	3	3.01 (0.331)	0.0355
C3	40	1.74 (0.722)	3	2.6 (0.18)	0.000339	30	1.75 (0.634)	3	2.46 (0.0626)	1.8e-06
C4	11	1.75 (0.461)	3	2.06 (0.175)	0.105	7	1.85 (0.401)	1	2.21 (NA)	
R1	56	3.52 (0.565)	3	2.25 (0.241)	0.00267	47	3.41 (0.503)	1	2.1 (NA)	
R2	56	3.3 (0.648)	3	1.93 (0.164)	2.15e-05	48	3.16 (0.566)	1	2.03 (NA)	
R3	56	2.93 (0.665)	3	1.27 (0.128)	1.54e-08	42	2.78 (0.599)	1	1.23 (NA)	

Reference sample: variations of main segments BSA-indexed diameters according to Syntax dominance in males.

	2D				p	3D				p
	right		left			right		left		
	n	mean (SD)	n	mean (SD)		n	mean (SD)	n	mean (SD)	
LM	53	2.28 (0.387)	5	2.37 (0.396)	0.659	44	2.15 (0.364)	4	2.44 (0.345)	0.19
L1	58	1.89 (0.344)	6	1.85 (0.169)	0.618	55	1.83 (0.311)	6	1.81 (0.155)	0.828
L2	58	1.45 (0.223)	6	1.43 (0.163)	0.791	53	1.4 (0.186)	6	1.4 (0.157)	0.98
L3	58	1.01 (0.191)	6	1.13 (0.176)	0.185	51	0.985 (0.182)	5	1.11 (0.166)	0.169
L4	46	0.643 (0.164)	6	0.778 (0.0921)	0.0127	28	0.632 (0.13)	4	0.694 (0.0874)	0.272
C1	58	1.71 (0.433)	6	1.94 (0.313)	0.149	53	1.61 (0.362)	6	1.93 (0.312)	0.0541

C2	54	1.29 (0.417)	6	1.69 (0.314)	0.0232	46	1.26 (0.333)	6	1.62 (0.348)	0.0507
C3	39	0.964 (0.407)	6	1.23 (0.134)	0.00433	30	0.928 (0.335)	5	1.26 (0.272)	0.0509
C4	11	0.995 (0.384)	6	0.95 (0.167)	0.741	6	0.996 (0.406)	3	0.987 (0.13)	0.964
R1	58	2.03 (0.343)	6	1.45 (0.0987)	2.99e-09	51	1.95 (0.332)	5	1.37 (0.123)	4.97e-06
R2	58	1.88 (0.398)	6	1.08 (0.197)	8.18e-06	50	1.79 (0.372)	5	1 (0.177)	2.94e-05
R3	57	1.64 (0.365)	6	0.632 (0.164)	7.16e-08	45	1.49 (0.291)	5	0.595 (0.127)	2.71e-07

Reference sample: variations of main segments BSA-indexed diameters according to Syntax dominance in females.

	2D				p	3D				p
	right		left			right		left		
	n	mean (SD)	n	mean (SD)		n	mean (SD)	n	mean (SD)	
LM	53	2.37 (0.361)	2	2.7 (0.488)		47	2.33 (0.302)	1	2.31 (NA)	
L1	56	2.02 (0.358)	3	1.8 (0.302)	0.326	52	1.98 (0.252)	3	1.8 (0.342)	0.47
L2	56	1.53 (0.347)	3	1.44 (0.0791)	0.228	53	1.5 (0.259)	3	1.37 (0.0947)	0.114
L3	55	0.985 (0.227)	3	1.17 (0.0742)	0.0216	52	0.988 (0.177)	3	1.11 (0.136)	0.26
L4	40	0.657 (0.135)	3	0.719 (0.0595)	0.202	31	0.663 (0.136)	1	0.759 (NA)	
C1	56	1.76 (0.362)	3	2.26 (0.296)	0.091	55	1.74 (0.314)	3	2.28 (0.147)	0.00942
C2	52	1.35 (0.429)	3	1.91 (0.103)	0.000196	49	1.31 (0.368)	3	1.84 (0.159)	0.0106
C3	40	1.03 (0.439)	3	1.6 (0.185)	0.011	30	1.03 (0.394)	3	1.51 (0.076)	2.1e-05
C4	11	1.04 (0.249)	3	1.26 (0.102)	0.0453	7	1.08 (0.231)	1	1.35 (NA)	
R1	56	2.07 (0.334)	3	1.38 (0.172)	0.0087	47	2 (0.309)	1	1.35 (NA)	
R2	56	1.94 (0.382)	3	1.19 (0.147)	0.00221	48	1.85 (0.339)	1	1.31 (NA)	

R3	56	1.72 (0.38)	3	0.784 (0.117)	0.000124	42	1.62 (0.346)	1	0.793 (NA)	

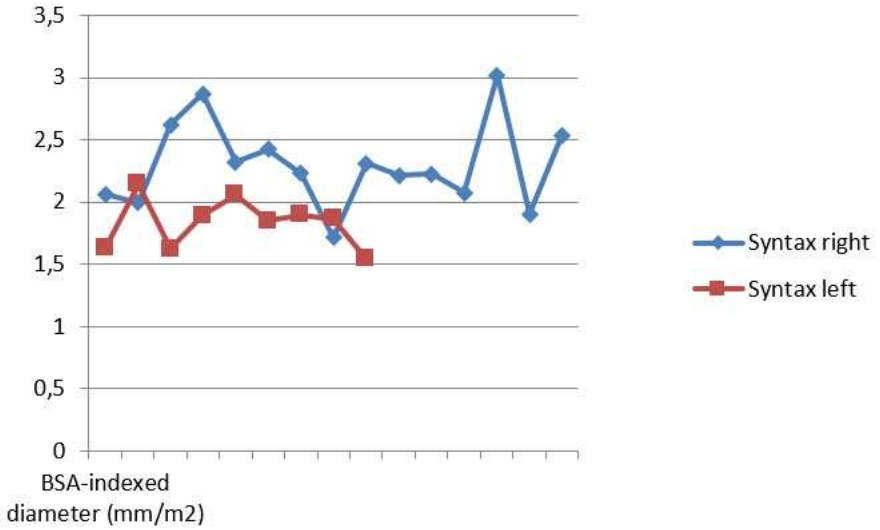
Reference sample: variations of main segments height-indexed diameters according to Syntax dominance in males.

	2D				p	3D				p
	right		left			right		left		
	n	mean (SD)	n	mean (SD)		n	mean (SD)	n	mean (SD)	
LM	53	2.55 (0.443)	5	2.63 (0.36)	0.685	44	2.39 (0.362)	4	2.7 (0.323)	0.154
L1	58	2.11 (0.376)	6	2.07 (0.226)	0.731	55	2.03 (0.317)	6	2.02 (0.153)	0.926
L2	58	1.62 (0.27)	6	1.61 (0.216)	0.867	53	1.56 (0.192)	6	1.57 (0.174)	0.93
L3	58	1.13 (0.226)	6	1.27 (0.238)	0.232	51	1.1 (0.205)	5	1.24 (0.231)	0.231
L4	46	0.72 (0.196)	6	0.875 (0.133)	0.0348	28	0.706 (0.154)	4	0.777 (0.13)	0.374
C1	58	1.92 (0.494)	6	2.17 (0.331)	0.134	53	1.79 (0.402)	6	2.16 (0.327)	0.0402
C2	54	1.44 (0.48)	6	1.89 (0.359)	0.0257	46	1.4 (0.377)	6	1.81 (0.396)	0.0524
C3	39	1.08 (0.447)	6	1.38 (0.166)	0.00709	30	1.04 (0.368)	5	1.43 (0.314)	0.0463
C4	11	1.12 (0.395)	6	1.07 (0.207)	0.728	6	1.11 (0.41)	3	1.13 (0.128)	0.891
R1	58	2.26 (0.348)	6	1.63 (0.127)	1.64e-07	51	2.17 (0.328)	5	1.52 (0.126)	2.91e-06
R2	58	2.09 (0.418)	6	1.21 (0.221)	1.24e-05	50	1.99 (0.372)	5	1.11 (0.182)	1.84e-05
R3	57	1.83 (0.38)	6	0.708 (0.185)	1.67e-07	45	1.67 (0.318)	5	0.66 (0.131)	6.05e-08

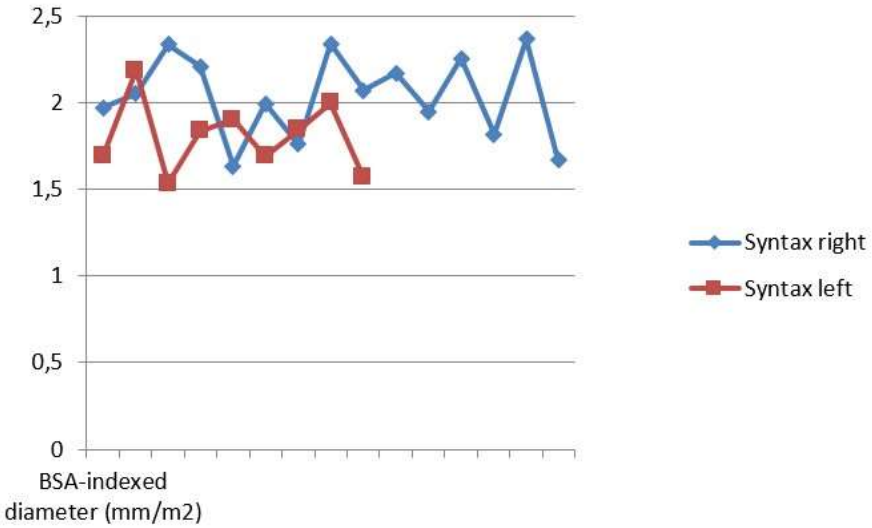
Reference sample: variations of main segments height-indexed diameters according to Syntax dominance in females.

	2D				p	3D				p
	right		left			right		left		
	n	mean (SD)	n	mean (SD)		n	mean (SD)	n	mean (SD)	
LM	53	2.43 (0.344)	2	2.8 (0.395)		47	2.4 (0.252)	1	2.47 (NA)	
L1	56	2.08 (0.365)	3	1.83 (0.307)	0.278	52	2.04 (0.242)	3	1.83 (0.33)	0.376
L2	56	1.58 (0.349)	3	1.46 (0.0118)	0.0228	53	1.54 (0.245)	3	1.39 (0.045)	0.00288
L3	55	1.02 (0.236)	3	1.18 (0.0729)	0.0259	52	1.02 (0.18)	3	1.12 (0.0878)	0.16
L4	40	0.68 (0.15)	3	0.732 (0.097)	0.459	31	0.677 (0.142)	1	0.735 (NA)	
C1	56	1.82 (0.388)	3	2.29 (0.196)	0.0349	55	1.79 (0.316)	3	2.32 (0.0924)	0.000461
C2	52	1.39 (0.442)	3	1.94 (0.139)	0.00315	49	1.35 (0.375)	3	1.87 (0.216)	0.0354
C3	40	1.06 (0.456)	3	1.62 (0.119)	0.000437	30	1.06 (0.402)	3	1.53 (0.0279)	5.9e-07
C4	11	1.06 (0.283)	3	1.28 (0.0996)	0.0569	7	1.13 (0.249)	1	1.37 (NA)	
R1	56	2.14 (0.338)	3	1.4 (0.159)	0.0051	47	2.07 (0.289)	1	1.31 (NA)	
R2	56	2 (0.389)	3	1.2 (0.109)	0.000104	48	1.92 (0.328)	1	1.27 (NA)	
R3	56	1.78 (0.396)	3	0.794 (0.0823)	1.27e-07	42	1.68 (0.349)	1	0.769 (NA)	

Reference sample: scatterplot showing BSA-indexed L1 (proximal LAD) 2D diameters variation according to Syntax dominances: right dominance (n = 114), left dominance (n = 9).



Reference sample: scatterplot showing BSA-indexed L1 (proximal LAD) 3D diameters variation according to Syntax dominances: right dominance (n = 107), left dominance (n = 9).



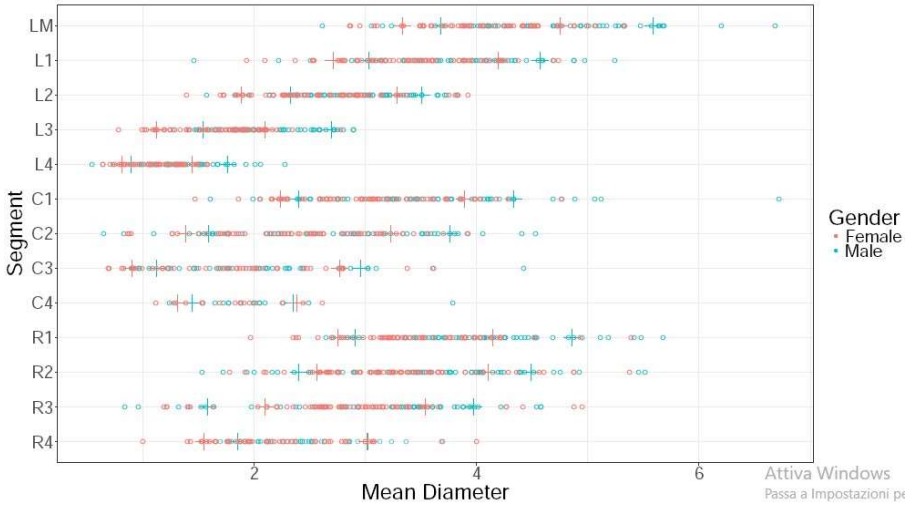
Reference sample: variations of main segments 2D diameters according to gender.

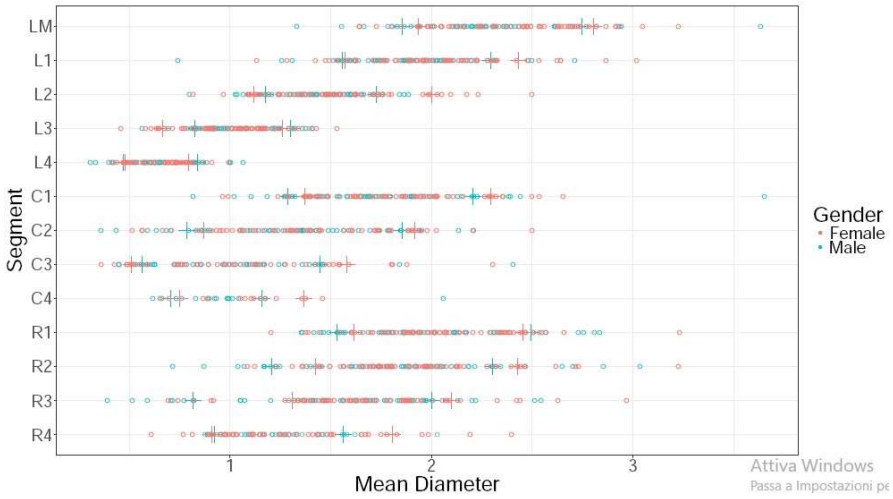
Coronary dominance	Main segments	Non-indexed 2D diameters			BSA-indexed 2D diameters			Height-indexed 2D diameters		
		men	women	p	men	women	p	men	women	p
Syntax right	LM	4.57 (0.807)	4.01 (0.567)	8.11e-05	2.28 (0.387)	2.37 (0.361)	0.254	2.55 (0.443)	2.43 (0.344)	0.117
	L1	3.78 (0.698)	3.44 (0.601)	0.00625	1.89 (0.344)	2.02 (0.358)	0.052	2.11 (0.376)	2.08 (0.365)	0.693
	L2	2.9 (0.508)	2.6 (0.574)	0.00322	1.45 (0.223)	1.53 (0.347)	0.161	1.62 (0.27)	1.58 (0.349)	0.416
	L3	2.03 (0.423)	1.68 (0.398)	1.45e-05	1.01 (0.191)	0.985 (0.227)	0.465	1.13 (0.226)	1.02 (0.236)	0.00862
	L4	1.29 (0.359)	1.13 (0.251)	0.0161	0.643 (0.164)	0.657 (0.135)	0.664	0.72 (0.196)	0.68 (0.15)	0.296
	C1	3.43 (0.885)	3.01 (0.651)	0.00433	1.71 (0.433)	1.76 (0.362)	0.504	1.92 (0.494)	1.82 (0.388)	0.247
	C2	2.58 (0.862)	2.3 (0.724)	0.0699	1.29 (0.417)	1.35 (0.429)	0.423	1.44 (0.48)	1.39 (0.442)	0.58
	C3	1.95 (0.778)	1.74 (0.722)	0.222	0.964 (0.407)	1.03 (0.439)	0.505	1.08 (0.447)	1.06 (0.456)	0.773
	C4	2.01 (0.65)	1.75 (0.461)	0.296	0.995 (0.384)	1.04 (0.249)	0.755	1.12 (0.395)	1.06 (0.283)	0.692
	R1	4.03 (0.644)	3.52 (0.565)	1.93e-05	2.03 (0.343)	2.07 (0.334)	0.443	2.26 (0.348)	2.14 (0.338)	0.0699
	R2	3.74 (0.74)	3.3 (0.648)	0.00113	1.88 (0.398)	1.94 (0.382)	0.378	2.09 (0.418)	2 (0.389)	0.233
	R3	3.27 (0.687)	2.93 (0.665)	0.00962	1.64 (0.365)	1.72 (0.38)	0.259	1.83 (0.38)	1.78 (0.396)	0.484
	R4	2.41 (0.468)	2.22 (0.613)	0.0922	1.22 (0.25)	1.31 (0.389)	0.204	1.35 (0.258)	1.35 (0.382)	0.945
Dodge right	LM	4.38 (0.724)	4.04 (0.648)	0.0445	2.24 (0.322)	2.37 (0.399)	0.14	2.47 (0.396)	2.46 (0.386)	0.867
	L1	3.64 (0.77)	3.59 (0.565)	0.769	1.86 (0.374)	2.1 (0.35)	0.00667	2.05 (0.413)	2.18 (0.342)	0.15
	L2	2.81 (0.549)	2.71 (0.579)	0.448	1.43 (0.24)	1.59 (0.365)	0.0413	1.58 (0.298)	1.65 (0.355)	0.436
	L3	1.92 (0.429)	1.69 (0.38)	0.0191	0.981 (0.2)	0.987 (0.219)	0.915	1.08 (0.236)	1.03 (0.227)	0.302
	L4	1.24 (0.414)	1.15 (0.26)	0.332	0.632 (0.193)	0.661 (0.131)	0.539	0.699 (0.232)	0.692 (0.153)	0.899
	C1	3.07 (0.753)	2.97 (0.62)	0.558	1.56 (0.343)	1.74 (0.375)	0.0451	1.73 (0.412)	1.8 (0.376)	0.419

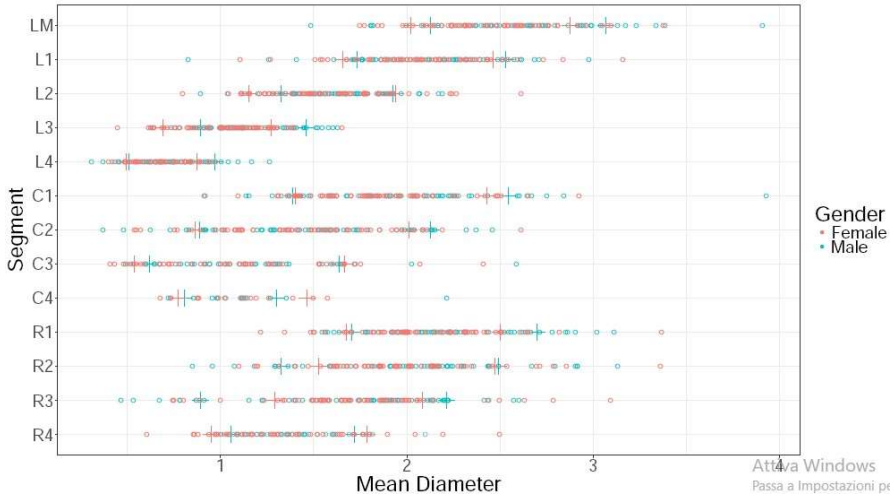
	C2	2.23 (0.761)	2.13 (0.765)	0.615	1.13 (0.372)	1.25 (0.463)	0.279	1.25 (0.428)	1.3 (0.48)	0.719
	C3	1.4 (0.491)	1.46 (0.741)	0.76	0.707 (0.253)	0.865 (0.467)	0.215	0.785 (0.29)	0.895 (0.489)	0.417
	R1	4.14 (0.685)	3.71 (0.563)	0.00528	2.12 (0.35)	2.17 (0.342)	0.544	2.33 (0.36)	2.25 (0.332)	0.337
	R2	3.96 (0.683)	3.54 (0.658)	0.0119	2.03 (0.372)	2.07 (0.396)	0.625	2.23 (0.383)	2.15 (0.392)	0.389
	R3	3.49 (0.561)	3.21 (0.63)	0.0552	1.79 (0.306)	1.88 (0.368)	0.271	1.97 (0.306)	1.95 (0.371)	0.83
	R4	2.49 (0.469)	2.41 (0.558)	0.534	1.28 (0.251)	1.42 (0.37)	0.0635	1.4 (0.26)	1.47 (0.35)	0.385
Dodge small right	LM	4.41 (0.759)	3.88 (0.437)	0.0916	2.07 (0.332)	2.28 (0.327)	0.185	2.41 (0.376)	2.34 (0.287)	0.647
	L1	3.91 (0.583)	3.16 (0.591)	0.00612	1.9 (0.317)	1.87 (0.351)	0.841	2.17 (0.323)	1.91 (0.348)	0.0837
	L2	3.11 (0.509)	2.36 (0.423)	0.000972	1.5 (0.232)	1.39 (0.231)	0.27	1.72 (0.251)	1.43 (0.24)	0.00962
	L3	2.16 (0.398)	1.63 (0.362)	0.00391	1.04 (0.162)	0.958 (0.199)	0.304	1.19 (0.19)	0.985 (0.209)	0.0265
	L4	1.38 (0.354)	1.08 (0.259)	0.0596	0.665 (0.14)	0.635 (0.174)	0.707	0.762 (0.169)	0.651 (0.164)	0.191
	C1	3.63 (0.408)	2.76 (0.43)	6.65e-05	1.76 (0.177)	1.62 (0.177)	0.0851	2.01 (0.208)	1.66 (0.223)	0.000974
	C2	2.84 (0.82)	2.22 (0.537)	0.0478	1.38 (0.387)	1.3 (0.277)	0.607	1.58 (0.45)	1.34 (0.291)	0.154
	C3	1.99 (0.415)	1.54 (0.382)	0.0167	0.968 (0.234)	0.906 (0.212)	0.52	1.1 (0.242)	0.929 (0.216)	0.0913
	R1	4.06 (0.268)	3.4 (0.46)	0.000776	1.97 (0.211)	2.01 (0.289)	0.713	2.25 (0.152)	2.06 (0.269)	0.0524
	R2	3.76 (0.321)	3.09 (0.422)	0.000433	1.82 (0.177)	1.82 (0.247)	0.986	2.08 (0.166)	1.86 (0.233)	0.0198
	R3	3.24 (0.446)	2.74 (0.304)	0.00484	1.57 (0.196)	1.62 (0.154)	0.509	1.79 (0.219)	1.66 (0.164)	0.0994
	R4	2.2 (0.404)	1.63 (0.34)	0.00149	1.06 (0.17)	0.962 (0.199)	0.224	1.21 (0.203)	0.985 (0.207)	0.0145
Dodge balanced	LM	5.35 (0.71)	4.05 (0.389)	0.000166	2.62 (0.46)	2.43 (0.257)	0.277	2.97 (0.446)	2.45 (0.245)	0.00641
	L1	4.06 (0.468)	3.22 (0.607)	0.00189	1.99 (0.274)	1.92 (0.345)	0.603	2.25 (0.274)	1.95 (0.377)	0.0495
	L2	2.96 (0.28)	2.48 (0.64)	0.039	1.45 (0.154)	1.48 (0.365)	0.833	1.64 (0.163)	1.5 (0.386)	0.293
	L3	2.22 (0.343)	1.69 (0.509)	0.0101	1.09 (0.183)	1.01 (0.29)	0.424	1.23 (0.196)	1.02 (0.302)	0.0709

	L4	1.33 (0.141)	1.12 (0.241)	0.0363	0.65 (0.0941)	0.665 (0.121)	0.771	0.737 (0.0869)	0.677 (0.141)	0.288
	C1	4.35 (0.951)	3.36 (0.814)	0.0161	2.15 (0.584)	1.98 (0.387)	0.437	2.42 (0.589)	2.03 (0.485)	0.103
	C2	3.29 (0.66)	2.84 (0.493)	0.0843	1.62 (0.368)	1.69 (0.265)	0.626	1.83 (0.392)	1.72 (0.288)	0.449
	C3	2.7 (0.805)	2.39 (0.514)	0.3	1.33 (0.466)	1.42 (0.289)	0.606	1.5 (0.484)	1.45 (0.321)	0.761
	C4	2.01 (0.65)	1.75 (0.461)	0.296	0.995 (0.384)	1.04 (0.249)	0.755	1.12 (0.395)	1.06 (0.283)	0.692
	R1	3.64 (0.697)	3.08 (0.386)	0.0331	1.78 (0.32)	1.83 (0.207)	0.634	2.02 (0.38)	1.87 (0.245)	0.286
	R2	3.01 (0.822)	2.78 (0.403)	0.414	1.46 (0.358)	1.66 (0.25)	0.155	1.66 (0.444)	1.68 (0.254)	0.904
	R3	2.51 (0.815)	2.26 (0.477)	0.412	1.23 (0.378)	1.35 (0.265)	0.417	1.39 (0.441)	1.37 (0.284)	0.911
Syntax & Dodge left	LM	4.61 (0.658)	4.51 (0.676)	0.875	2.37 (0.396)	2.7 (0.488)	0.501	2.63 (0.36)	2.8 (0.395)	0.655
	L1	3.68 (0.491)	2.94 (0.515)	0.109	1.85 (0.169)	1.8 (0.302)	0.8	2.07 (0.226)	1.83 (0.307)	0.297
	L2	2.85 (0.436)	2.35 (0.0337)	0.0392	1.43 (0.163)	1.44 (0.0791)	0.882	1.61 (0.216)	1.46 (0.0118)	0.17
	L3	2.25 (0.463)	1.9 (0.13)	0.137	1.13 (0.176)	1.17 (0.0742)	0.658	1.27 (0.238)	1.18 (0.0729)	0.451
	L4	1.55 (0.265)	1.18 (0.153)	0.0336	0.778 (0.0921)	0.719 (0.0595)	0.285	0.875 (0.133)	0.732 (0.097)	0.121
	C1	3.84 (0.66)	3.67 (0.326)	0.626	1.94 (0.313)	2.26 (0.296)	0.204	2.17 (0.331)	2.29 (0.196)	0.531
	C2	3.35 (0.686)	3.11 (0.206)	0.453	1.69 (0.314)	1.91 (0.103)	0.174	1.89 (0.359)	1.94 (0.139)	0.803
	C3	2.45 (0.37)	2.6 (0.18)	0.455	1.23 (0.134)	1.6 (0.185)	0.0542	1.38 (0.166)	1.62 (0.119)	0.0547
	C4	1.89 (0.412)	2.06 (0.175)	0.432	0.95 (0.167)	1.26 (0.102)	0.0124	1.07 (0.207)	1.28 (0.0996)	0.0761
	R1	2.88 (0.269)	2.25 (0.241)	0.0187	1.45 (0.0987)	1.38 (0.172)	0.542	1.63 (0.127)	1.4 (0.159)	0.11
	R2	2.13 (0.411)	1.93 (0.164)	0.337	1.08 (0.197)	1.19 (0.147)	0.385	1.21 (0.221)	1.2 (0.109)	0.988
	R3	1.25 (0.311)	1.27 (0.128)	0.855	0.632 (0.164)	0.784 (0.117)	0.164	0.708 (0.185)	0.794 (0.0823)	0.367

Reference sample: scatterplots showing non-, BSA- and height-indexed main segments 2D diameters variation according to gender.







Reference sample: variations of main segments 3D diameters according to gender.

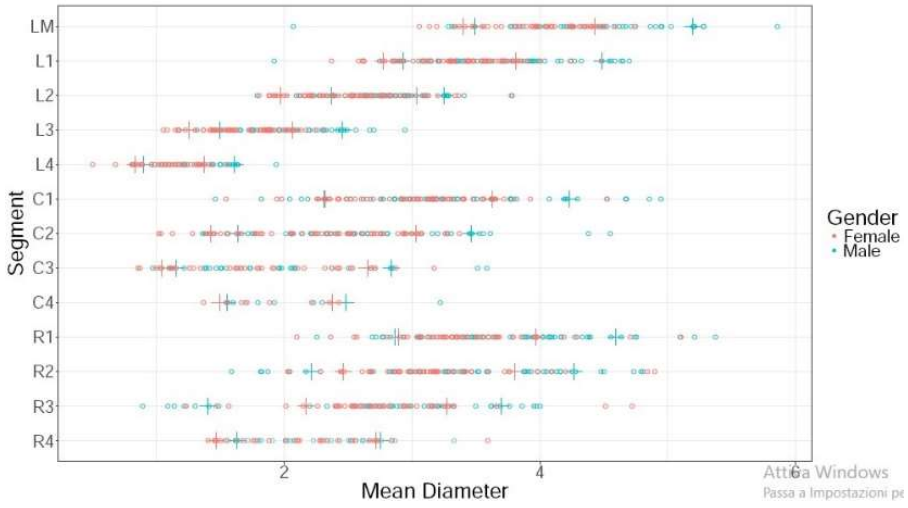
Coronary dominance	Main segments	Non-indexed 3D diameters			BSA-indexed 3D diameters			Height-indexed 3D diameters		
		men	women	p	men	women	p	men	women	p
Syntax right	LM	4.29 (0.671)	3.97 (0.411)	0.00755	2.15 (0.364)	2.33 (0.302)	0.0122	2.39 (0.362)	2.4 (0.252)	0.877
	L1	3.63 (0.584)	3.37 (0.419)	0.00934	1.83 (0.311)	1.98 (0.252)	0.00579	2.03 (0.317)	2.04 (0.242)	0.797
	L2	2.79 (0.359)	2.54 (0.419)	0.00148	1.4 (0.186)	1.5 (0.259)	0.0255	1.56 (0.192)	1.54 (0.245)	0.716
	L3	1.96 (0.375)	1.67 (0.313)	7.58e-05	0.985 (0.182)	0.988 (0.177)	0.945	1.1 (0.205)	1.02 (0.18)	0.0419
	L4	1.26 (0.286)	1.11 (0.236)	0.0365	0.632 (0.13)	0.663 (0.136)	0.376	0.706 (0.154)	0.677 (0.142)	0.45
	C1	3.2 (0.74)	2.95 (0.536)	0.0547	1.61 (0.362)	1.74 (0.314)	0.0527	1.79 (0.402)	1.79 (0.316)	0.989
	C2	2.51 (0.68)	2.23 (0.621)	0.0422	1.26 (0.333)	1.31 (0.368)	0.443	1.4 (0.377)	1.35 (0.375)	0.517
	C3	1.86 (0.642)	1.75 (0.634)	0.515	0.928 (0.335)	1.03 (0.394)	0.283	1.04 (0.368)	1.06 (0.402)	0.834
	C4	1.98 (0.663)	1.85 (0.401)	0.701	0.996 (0.406)	1.08 (0.231)	0.668	1.11 (0.41)	1.13 (0.249)	0.888
	R1	3.88 (0.595)	3.41 (0.503)	5.71e-05	1.95 (0.332)	2 (0.309)	0.433	2.17 (0.328)	2.07 (0.289)	0.107
	R2	3.56 (0.643)	3.16 (0.566)	0.00146	1.79 (0.372)	1.85 (0.339)	0.367	1.99 (0.372)	1.92 (0.328)	0.281

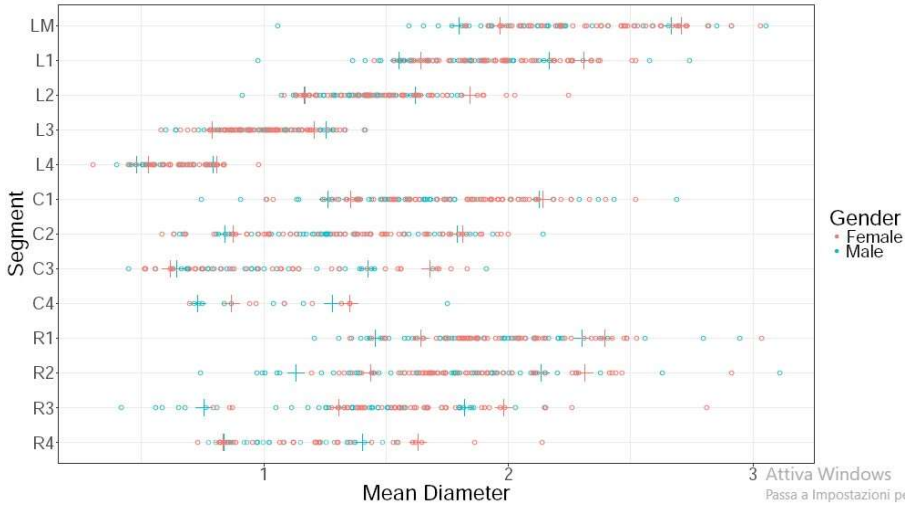
	R3	2.99 (0.576)	2.78 (0.599)	0.0972	1.49 (0.291)	1.62 (0.346)	0.06	1.67 (0.318)	1.68 (0.349)	0.865
	R4	2.21 (0.461)	2.12 (0.539)	0.48	1.12 (0.236)	1.24 (0.353)	0.137	1.24 (0.25)	1.28 (0.328)	0.57
Dodge right	LM	4.2 (0.636)	3.94 (0.417)	0.0643	2.16 (0.359)	2.29 (0.278)	0.136	2.37 (0.355)	2.39 (0.246)	0.809
	L1	3.55 (0.623)	3.43 (0.425)	0.362	1.83 (0.335)	2 (0.248)	0.019	2 (0.341)	2.08 (0.238)	0.294
	L2	2.71 (0.338)	2.58 (0.454)	0.184	1.4 (0.196)	1.51 (0.278)	0.0594	1.53 (0.197)	1.57 (0.263)	0.556
	L3	1.84 (0.339)	1.65 (0.342)	0.0288	0.947 (0.184)	0.964 (0.183)	0.71	1.04 (0.198)	1 (0.193)	0.432
	L4	1.19 (0.282)	1.09 (0.255)	0.272	0.612 (0.131)	0.633 (0.13)	0.625	0.674 (0.16)	0.656 (0.146)	0.742
	C1	2.85 (0.592)	2.9 (0.496)	0.698	1.47 (0.294)	1.7 (0.31)	0.00297	1.61 (0.322)	1.76 (0.293)	0.0545
	C2	2.22 (0.543)	2.07 (0.624)	0.35	1.14 (0.291)	1.21 (0.377)	0.454	1.25 (0.314)	1.26 (0.386)	0.97
	C3	1.46 (0.469)	1.48 (0.573)	0.942	0.756 (0.242)	0.869 (0.366)	0.378	0.834 (0.283)	0.904 (0.388)	0.612
	R1	4.05 (0.599)	3.56 (0.535)	0.00203	2.08 (0.336)	2.07 (0.333)	0.9	2.28 (0.326)	2.16 (0.299)	0.137
	R2	3.78 (0.544)	3.36 (0.6)	0.00783	1.94 (0.349)	1.96 (0.363)	0.892	2.13 (0.33)	2.04 (0.341)	0.29
	R3	3.22 (0.465)	3.04 (0.569)	0.241	1.63 (0.229)	1.77 (0.335)	0.0984	1.81 (0.252)	1.84 (0.324)	0.691
	R4	2.29 (0.444)	2.23 (0.512)	0.66	1.17 (0.233)	1.31 (0.338)	0.12	1.29 (0.243)	1.35 (0.307)	0.453
Dodge small right	LM	4.19 (0.715)	3.86 (0.424)	0.278	1.95 (0.27)	2.25 (0.271)	0.0398	2.27 (0.332)	2.31 (0.266)	0.783
	L1	3.69 (0.518)	3.18 (0.518)	0.0441	1.78 (0.262)	1.88 (0.306)	0.46	2.04 (0.263)	1.93 (0.298)	0.415
	L2	2.97 (0.454)	2.37 (0.36)	0.00429	1.43 (0.174)	1.42 (0.21)	0.976	1.63 (0.201)	1.45 (0.211)	0.0619
	L3	2.2 (0.429)	1.64 (0.269)	0.00354	1.06 (0.175)	0.986 (0.164)	0.366	1.21 (0.21)	1 (0.164)	0.0274
	L4	1.41 (0.333)	1.17 (0.287)	0.2	0.668 (0.129)	0.708 (0.194)	0.687	0.773 (0.155)	0.717 (0.186)	0.586
	C1	3.48 (0.433)	2.73 (0.469)	0.00124	1.68 (0.192)	1.61 (0.238)	0.444	1.92 (0.213)	1.65 (0.265)	0.0199
	C2	2.66 (0.822)	2.19 (0.543)	0.141	1.28 (0.377)	1.28 (0.269)	0.998	1.47 (0.441)	1.32 (0.29)	0.374
	C3	1.84 (0.509)	1.46 (0.337)	0.0883	0.906 (0.268)	0.856 (0.198)	0.667	1.02 (0.284)	0.882 (0.191)	0.244

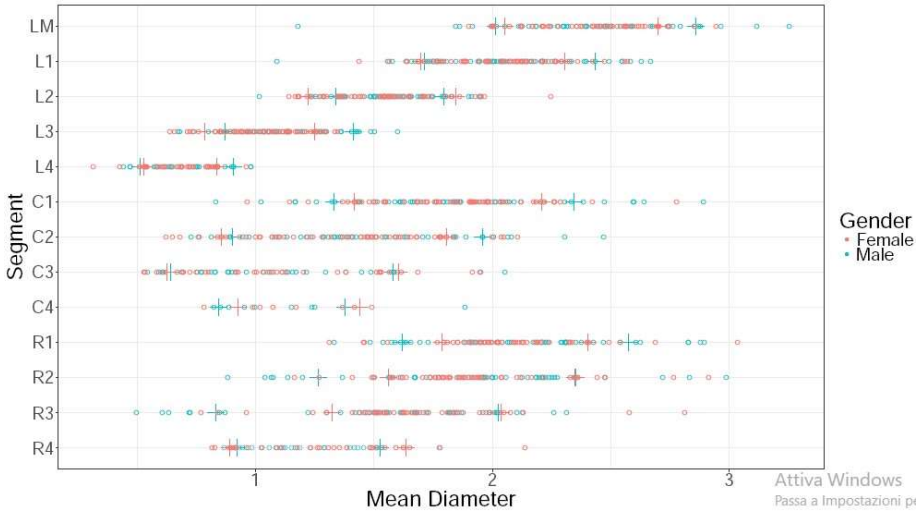
	R1	3.95 (0.381)	3.26 (0.443)	0.00125	1.9 (0.201)	1.92 (0.244)	0.825	2.18 (0.187)	1.97 (0.246)	0.0444
	R2	3.6 (0.485)	2.96 (0.375)	0.00437	1.72 (0.195)	1.74 (0.186)	0.819	1.98 (0.229)	1.79 (0.189)	0.0592
	R3	3.01 (0.327)	2.59 (0.311)	0.0136	1.44 (0.139)	1.51 (0.124)	0.303	1.66 (0.16)	1.56 (0.162)	0.211
	R4	1.95 (0.445)	1.62 (0.367)	0.173	0.938 (0.145)	0.914 (0.222)	0.837	1.07 (0.204)	0.968 (0.238)	0.45
Dodge balanced	LM	4.77 (0.649)	4.16 (0.358)	0.0511	2.32 (0.415)	2.51 (0.348)	0.341	2.63 (0.373)	2.52 (0.237)	0.527
	L1	3.8 (0.525)	3.33 (0.256)	0.0192	1.86 (0.302)	2 (0.217)	0.267	2.11 (0.305)	2.03 (0.187)	0.498
	L2	2.83 (0.257)	2.57 (0.327)	0.0574	1.39 (0.182)	1.54 (0.24)	0.135	1.57 (0.165)	1.56 (0.205)	0.932
	L3	2.1 (0.273)	1.78 (0.24)	0.0172	1.04 (0.161)	1.07 (0.163)	0.718	1.17 (0.162)	1.09 (0.14)	0.247
	L4	1.32 (0.186)	1.13 (0.144)	0.103	0.658 (0.138)	0.701 (0.0844)	0.565	0.736 (0.121)	0.694 (0.0895)	0.533
	C1	4 (0.697)	3.33 (0.568)	0.027	1.98 (0.432)	1.98 (0.281)	0.979	2.23 (0.422)	2.01 (0.338)	0.22
	C2	3.07 (0.395)	2.75 (0.394)	0.0859	1.52 (0.241)	1.64 (0.232)	0.266	1.71 (0.238)	1.67 (0.242)	0.7
	C3	2.31 (0.661)	2.4 (0.432)	0.724	1.14 (0.384)	1.42 (0.29)	0.0877	1.28 (0.396)	1.45 (0.294)	0.315
	C4	1.98 (0.663)	1.85 (0.401)	0.701	0.996 (0.406)	1.08 (0.231)	0.668	1.11 (0.41)	1.13 (0.249)	0.888
	R1	3.38 (0.511)	3.14 (0.283)	0.199	1.65 (0.204)	1.87 (0.249)	0.0508	1.87 (0.271)	1.91 (0.211)	0.739
	R2	2.89 (0.636)	2.81 (0.384)	0.745	1.4 (0.261)	1.69 (0.305)	0.0362	1.6 (0.339)	1.71 (0.259)	0.415
	R3	2.34 (0.618)	2.23 (0.439)	0.688	1.13 (0.266)	1.31 (0.283)	0.182	1.29 (0.326)	1.36 (0.276)	0.64
Syntax & Dodge left	LM	4.69 (0.528)	3.96 (NA)	NaN	2.44 (0.345)	2.31 (NA)	NaN	2.7 (0.323)	2.47 (NA)	NaN
	L1	3.58 (0.372)	2.94 (0.553)	0.169	1.81 (0.155)	1.8 (0.342)	0.986	2.02 (0.153)	1.83 (0.33)	0.419
	L2	2.78 (0.357)	2.23 (0.0876)	0.0123	1.4 (0.157)	1.37 (0.0947)	0.732	1.57 (0.174)	1.39 (0.045)	0.0551
	L3	2.18 (0.416)	1.8 (0.147)	0.119	1.11 (0.166)	1.11 (0.136)	0.977	1.24 (0.231)	1.12 (0.0878)	0.334
	L4	1.38 (0.262)	1.18 (NA)	NaN	0.694 (0.0874)	0.759 (NA)	NaN	0.777 (0.13)	0.735 (NA)	NaN
	C1	3.82 (0.651)	3.72 (0.176)	0.742	1.93 (0.312)	2.28 (0.147)	0.0541	2.16 (0.327)	2.32 (0.0924)	0.308

	C2	3.21 (0.754)	3.01 (0.331)	0.59	1.62 (0.348)	1.84 (0.159)	0.23	1.81 (0.396)	1.87 (0.216)	0.778
	C3	2.53 (0.624)	2.46 (0.0626)	0.825	1.26 (0.272)	1.51 (0.076)	0.109	1.43 (0.314)	1.53 (0.0279)	0.509
	C4	2 (0.264)	2.21 (NA)	NaN	0.987 (0.13)	1.35 (NA)	NaN	1.13 (0.128)	1.37 (NA)	NaN
	R1	2.68 (0.249)	2.1 (NA)	NaN	1.37 (0.123)	1.35 (NA)	NaN	1.52 (0.126)	1.31 (NA)	NaN
	R2	1.94 (0.281)	2.03 (NA)	NaN	1 (0.177)	1.31 (NA)	NaN	1.11 (0.182)	1.27 (NA)	NaN
	R3	1.15 (0.189)	1.23 (NA)	NaN	0.595 (0.127)	0.793 (NA)	NaN	0.66 (0.131)	0.769 (NA)	NaN

Reference sample: scatterplots showing non-, BSA- and height-indexed main segments 3D diameters variation according to gender.




LM
L1
L2
L3
L4
C1
C2
C3
C4
R1
R2
R3
R4
Segment
1
2
3
Mean Diameter
Gender
Female
Male
Attiva Windows
Passa a Impostazioni p


LM
L1
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L3
L4
C1
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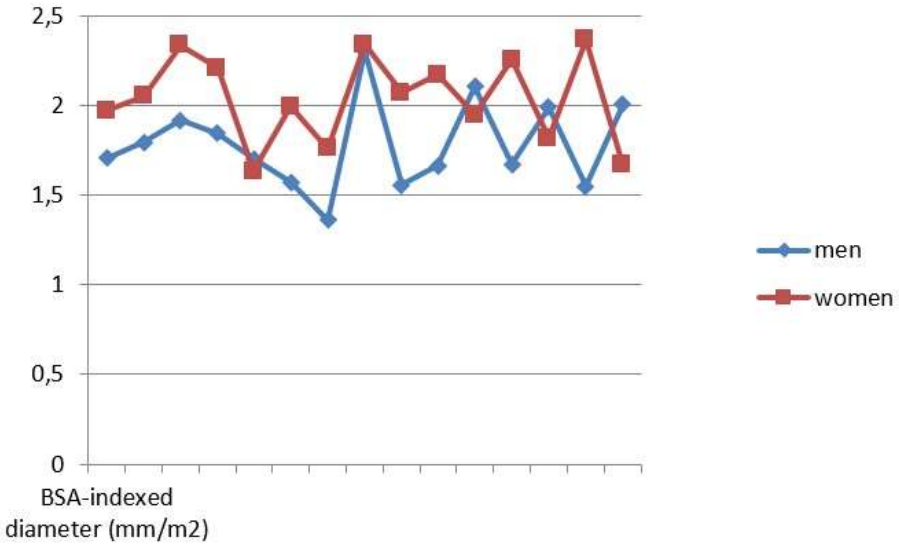
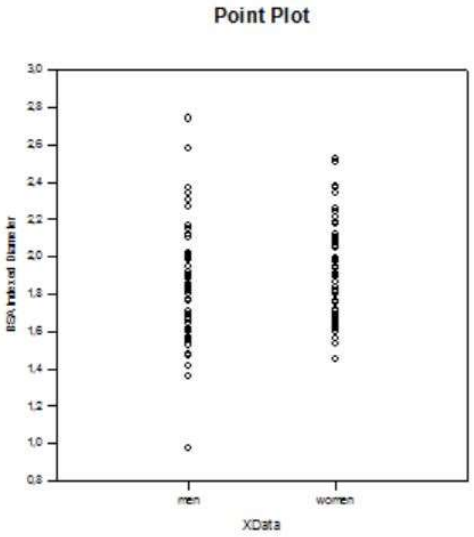
C3
C4
R1
R2
R3
R4
Segment
1
2
3
Mean Diameter
Gender
Female
Male
Attiva Windows
Passa a Impostazioni p

Reference sample: scatterplot showing BSA-indexed L1 (proximal LAD) 3D diameters variation according to gender: men (n = 61), women (n = 55).



Reference sample: point plot showing BSA-indexed L1 (proximal LAD) 3D diameters variation according to gender; p =0,006.



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CHAPTER 14

Discussion and conclusion

It is not that easy to justify a PhD program that covers all areas of interventional cardiology itself, in fact most researchers focus their scientific interests mainly on one or few main topics. However it must be said that these sectors present many interconnections between them, but also with other fields of medicine; for example, how could we good TAVI operators without being technically able to manage access site or coronary, as well as without possessing the necessary cultural background to manage potential periprocedural heart rhythm disorders or renal insufficiency? Although operators more than researchers have the ambition to range throughout all interventional cardiology, it should not be forgotten that research represents the basis for the development and improvement of all techniques, devices, drugs and skills. Facing an argument from the very beginning, which means from its definition, particularly from the definition of anatomical normality, is as uncommon as fundamental to acquire the right mindset to look at the coronary arteries from a perspective that is not only purely therapeutic. Collaboration with researchers whose scientific strengths belong to

different sectors of interventional cardiology can not help reinforcing and stimulating these ideas. It is for all these reasons that the research path started in the contest of my doctorate could be considered tiring and a bit distracting but in return absolutely educational for the open-mindedness that all operators should acquire.

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in collaboration with the University of Naples "Federico II" (Prof. Bruno Trimarco)

- ***SINCE NOVEMBER 2017*** **INTERNATIONAL PHD FELLOWSHIP** in **"CARDIOVASCULAR PATHOPHYSIOLOGY AND THERAPEUTICS"** (curriculum: interventional cardiology) at the **CARDIAC CATHETERIZATION LABORATORY** (Prof. Marco Valgimigli) of the **INSELSPITAL UNIVERSITY HOSPITAL – BERN (SWITZERLAND)**, in collaboration with the University of Naples "Federico II" (Prof. Bruno Trimarco)

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- ***OCTOBER 2015 – JANUARY 2016*** **CONSULTANT CARDIOLOGIST** at the public Hospital of Imperia (Dr. Roberto Mureddu) – **IMPERIA (ITALY)**
- ***FEBRUARY 2016 – OCTOBER 2017*** **CONSULTANT INTERVENTIONAL CARDIOLOGIST** at the Cardiac Catheterization Laboratory (Dr. Leonardo Abbracciavento) of the **"SS. ANNUNZIATA" HOSPITAL** of Taranto (Dr. Vitantonio Russo) – **TARANTO (ITALY)**
- ***SINCE JULY 2018*** **CONSULTANT INTERVENTIONAL CARDIOLOGIST** at the Cardiac Catheterization Laboratory (Dr. Donato Quagliara) of the **POLICLINICO UNIVERSITY HOSPITAL** of Bari (Prof. Stefano Favale) – **BARI (ITALY)**

Theoretical and practical courses

- *Basic Life Support and Defibrillation*, organized by the Italian Resuscitation Council. May 4, 2007, Bari (Italy)
- *Scaffold bioassorbibili: le indicazioni, i risultati e i segreti per l'impianto ottimale*, organized by "Magna Graecia" University of Catanzaro in collaboration with Abbott Vascular. April 4, 2013, Catanzaro (Italy)
- *Therapy of in-stent-restenoses, bifurcational lesions and small vessel disease with the Drug Eluting Balloon Technology*, organized by Klinikum Ernst von Bergmann of Potsdam in collaboration with B Braun. February 21, 2014, Potsdam (Germany)
- *ACURATE neo™/TF™ New Site Training*, organized by Deutsches Herzzentrum of Munich in collaboration with Symetis. September 10-11, 2015, Munich (Germany)

- *Ottimizzazione della rivascolarizzazione coronarica: valutazione funzionale e morfologica*, organized by "Montevergine" Clinic of Mercogliano in collaboration with Boston Scientific. September 11-12, 2017, Mercogliano (Italy)
- *Radial approach: the essentials (new)*, organized by the PCR edu online Proctoring Teams in collaboration with Terumo Medical Corporation. June 23, 2018
- *How to treat patients with undilatable/calcified coronary artery lesions?*, organized by the PCR edu online Proctoring Teams in collaboration with Boston Scientific. June 24, 2018
- *Medis QFR Training Course*, organized by Medis medical imaging systems bv. June 26-27, 2018, Leiden (The Netherlands)
- *Management of a patient presenting with complex multivessel coronary artery disease*, organized by PCR in collaboration with Medtronic. March 12-13, 2019, Madrid (Spain)
- *Italy: coronary and structural heart technologies*, organized by Medtronic. May 9, 2019, Galway (Ireland)
- *National implanters meeting*, organized by Medtronic. June 6-7, 2019, Rome (Italy)

Lectures

- Teaching of **SPORTS CARDIOLOGY**, A.Y. 2018-2019 (3° year 1° semester) – Integrated Course in Sports Cardiology – Degree Course in **SCIENCES OF MOTOR AND SPORT ACTIVITIES** – School of Medicine of the **UNIVERSITY OF BARI "ALDO MORO"**

Scientific activity

- **PUBLICATIONS**
  - **ORIGINAL ARTICLES**
    1. **Iacovelli F**, Scicchitano P, Zanna D, Marangelli V, Favale S. *Left ventricle outflow tract vegetation, embolism and troponin rise: an infective endocarditis case report*. INTERN EMERG MED. 2012 Sep;7 Suppl 2:S145-7.
    2. Pepe M, **Iacovelli F**, Masi F, Marangelli V, Scardapane A, De Santis A, Sgarra L, Quagliara D, Favale S. *Aortic coarctation: guidelines mismatch across the ocean*. J CARDIOTHORAC SURG. 2014 Feb 20:9(1):38.
    3. Pepe M, Furgieri A, Miranda M, Cafaro A, Paradies V, **Iacovelli F**, Castriota F, Liso A. *Emergency coronary & peripheral arteries*

combined percutaneous intervention in elderly: success or therapeutic excess? FUTURE CARDIOL. 2015 Sep;11(5):521-4.

4. **Iacovelli F**, Pepe M, Contegiacomo G, Alberotanza V, Masi F, Bortone AS, Favale S. *A striking coronary artery pattern in a grown-up congenital heart disease patient*. CASE REP CARDIOL. 2016;2016:5482578.
5. Bartolomucci F, Cecere A, Navarese EP, **Iacovelli F**, Cafaro A, Ciccone MM, Pepe M. *Giant cardiac fibroma in a completely asymptomatic teenager*. J CLIN EXP CARDIOLOG. 2016 Oct;7(10):469.
6. Pepe M, Cecere A, Napodano M, Ciccone MM, Bartolomucci F, Navarese EP, **Iacovelli F**, Zanna D, Mele M. *How to approach a spontaneous coronary artery dissection: an up-to-date*. INTERV CARDIOL J. 2017;3:1.
7. Cioppa A, Stabile E, Salemme L, Popusoi G, Pucciarelli A, **Iacovelli F**, Arcari A, Coscioni E, Trimarco B, Esposito G, Tesorio T. *Combined use of directional atherectomy and drug-coated balloon for the endovascular treatment of common femoral artery disease: immediate and one-year outcomes*. EUROINTERVENTION. 2017 Feb 20:12(14):1789-94.
8. Dachille A, **Iacovelli F**, Giardinelli F, De Cillis E, Signore N, Ciccone MM, Favale S, Contegiacomo G, Bortone AS. *Dissezione aortica acuta durante tentativo inefficace di impianto transcatetere di protesi aortica totalmente riposizionabile e recuperabile*. G ITAL CARDIOL. 2017;18(2 Suppl 1):31S-34S.
9. Bartolomucci F, Tito A, Navarese EP, **Iacovelli F**, Mele M, Larosa C, Ciccone MM, Cassese M, Pepe M. *STEMI and NSTEMI ACS in a 30-year-old patient: an extremely rare complication of a left atrial myxoma*. HEART SURG FORUM. 2017;Jun 30;20(3):E116-E118.
10. Barbanti M, Baan J, Spence MS, **Iacovelli F**, Martinelli GL, Saia F, Bortone AS, Van der Kley F, Muir DF, Densem CG, Vis M, Van Mourik MS, Seilerova L, Lüske CM, Bramlage P, Tamburino C. *Feasibility and safety of early discharge after transfemoral transcatheter aortic valve implantation – rationale and design of the FAST-TAVI registry*. BMC CARDIOVASC DISORD. 2017;Oct 10;17(1):259
11. **Iacovelli F**, Pignatelli A, Giugliano G, Stabile E, Cicala M, Salemme L, Cioppa A, Popusoi G, Pucciarelli A, Verdoliva S, Bortone AS, Losi M, Coscioni E, Esposito G, Contegiacomo G, Tesorio T. *Prosthesis depth and conduction disturbances after last generation balloon-expandable transcatheter aortic valve implantation*. EUROPACE. 2018;Jan 1;20(1):116-123.

12. Pucciarelli A, Arcari A, Popusoi G, Cioppa A, Salemme L, **Iacovelli F**, Napolitano G, Esposito G, Tesorio T, Stabile E. *Incidence and predictors of acute kidney injury in patients undergoing proximal protected carotid artery stenting*. EUROINTERVENTION. 2018;Jun 8;14(3):e360-e366.

13. Barbanti M, Van Mourik MS, Spence MS, **Iacovelli F**, Martinelli GL, Muir DF, Saia F, Bortone AS, Densem CG, Van der Kley F, Bramlage P, Vis M, Tamburino C. *Optimizing patient discharge management after transfemoral transcatheter aortic valve implantation: the multicentre european FAST-TAVI trial*. EUROINTERVENTION. 2019;Feb 19. pii: EIJ-D-18-01197. doi: 10.4244/EIJ-D-18-01197.

- **COLLABORATORSHIPS**

1. Eggebrecht H, Vaquerizo B, Moris C, Bossone E, Lämmer J, Czerny M, Zierer A, Schröfel H, Kim WK, Walther T, Scholtz S, Rudolph T, Hengstenberg C, Kempfert J, Spaziano M, Lefevre T, Bleiziffer S, Schofer J, Mehilli J, Seiffert M, Naber C, Biancari F, Eckner D, Cornet C, Lhermusier T, Philippart R, Siljander A, Cerillo AG, Blackman D, Chieffo A, Kahlert P, Czerwinska-Jelonkiewicz K, Szymanski P, Landes U, Kornowski R, D'Onofrio A, Kaulfersch C, Søndergaard L, Mylotte D, Mehta RH, De Backer O; European Registry on Emergent Cardiac Surgery during TAVI (EuRECS-TAVI). *Incidence and outcomes of emergent cardiac surgery during transfemoral transcatheter aortic valve implantation (TAVI): insights from the European Registry on Emergent Cardiac Surgery during TAVI (EuRECS-TAVI)*. EUR HEART J. 2018;Feb 21;39(8):676-684.

2. Tebaldi M, Biscaglia S, Fineschi M, Musumeci G, Marchese A, Leone AM, Rossi ML, Stefanini G, Maione A, Menozzi A, Tarantino F, Lodolini V, Gallo F, Barbato E, Tarantini G, Campo G. *Evolving routine standards in invasive hemodynamic assessment of coronary stenosis. The nationwide italian SICI-GISE cross-sectional ERIS study*. JACC CARDIOVASC INTERV. 2018;Aug 13;11(15):1482-1491.

- **ABSTRACTS (INTERNATIONAL CONGRESSES)**

1. C Caiati, ME Lepera, D Santoro, D Grande, **F Iacovelli**, N Tarantino, A Tito, I Lacitignola, M Basile, F Masi, S Favale. *Assessment of the Severity of Left Anterior Descending Coronary Artery Stenoses Using Transthoracic Enhanced Doppler Echocardiography in Convergent Color Doppler Mode: Validation of a Method Based on the Continuity Equation.* Proceedings of the 62ND ACC CONGRESS. March 9–11, 2013, San Francisco, USA (poster). JACC. 2013;61(10):A1027

2. C Caiati, ME Lepera, D Santoro, **F Iacovelli**, D Grande, A Tito, N Tarantino, A De Santis, F Masi, S Favale. *Distinguishing Ischemic from Non-Ischemic Left Bundle Branch Block by Transthoracic Enhanced Coronary Echo Doppler in Convergent Color Doppler Mode.* Proceedings of the 62ND ACC CONGRESS. March 9–11, 2013, San Francisco, USA (oral contribution). JACC. 2013;61(10):A1168

3. **F Iacovelli**, P Scicchitano, L Compostella, N Russo, P Guida, T Setzu, F Bellotto, S Favale. *Endothelial function amelioration after cardiological rehabilitation.* Proceedings of the EUROPREVENT CONGRESS 2013. April 18–20, 2013, Rome, Italy (poster). EUR J PREV CARDIOL. 2013;20 Suppl 1:S27

4. P Scicchitano, **F Iacovelli**, L Compostella, N Russo, P Guida, T Setzu, F Bellotto, S Favale. *Endothelial function and insulin-resistance: the role of cardiac rehabilitation.* Proceedings of the EUROPREVENT CONGRESS 2013. April 18–20, 2013, Rome, Italy (poster). EUR J PREV CARDIOL. 2013;20 Suppl 1:S101

5. C Caiati, ME Lepera, D Santoro, D Grande, A Tito, P Marolla, M Stufano, G Meliota, **F Iacovelli**, F Masi, S Favale. *Physiologic Significance Assessment of Intermediate Severity Coronary Lesions by Transthoracic Enhanced Doppler Echocardiography in Convergent Color Doppler Mode: Validation versus Fractional Flow Reserve.* Proceedings of the 63RD ACC CONGRESS. March 29–31, 2014, Washington, USA (poster). JACC. 2014;63(12_S):A1623

6. M Pepe, V Paradies, AS Bortone, E De Cillis, A Cafaro, **F Iacovelli**, T Acquaviva, F Masi, D Quagliara, S Favale. *"Broken-heart" syndrome: ventricular septal perforation in a tako-tsubo cardiomyopathy.* Proceedings of the ASIAPCR CONGRESS 2015. January 22–24, 2015, Singapore (clinical case).

7. A Pignatelli, **F Iacovelli**, G Giugliano, M Cicala, A Dachille, A Cioppa, A Pucciarelli, E Stabile, V Pestrichella, AS Bortone, T Tesorio, P Rubino, G Contegiacomo. *Impact of prosthesis implantation depth on atrioventricular and intraventricular conduction and pacemaker implantation rates after latest generation balloon-expandable TAVI.* Proceedings of the EUROPCR CONGRESS 2015. May 19–22, 2015, Paris, France (oral contribution).

8. M Cicala, **F Iacovelli**, G Giugliano, A Pignatelli, F Giardinelli, L Salemme, S Verdoliva, G Popusoi, E Stabile, AS Bortone, T Tesorio, V Pestrichella, G Contegiacomo. *Impact of contrast mean osmolality on the risk of contrast-induced nephropathy after TAVI.* Proceedings of the EUROPCR CONGRESS 2015. May 19–22, 2015, Paris, France (poster).

9. **F Iacovelli**, G Giugliano, AS Bortone, M Cicala, A Pignatelli, E Stabile, R Alemanni, R Montesanti, A Cotroneo, G Martinelli, M Cassese, G Contegiacomo, T Tesorio. *The haemodynamic performance of the aortic bioprosthesis in the elderly: a comparison between transcatheter and sutureless implantation.* Proceedings of the EUROPCR CONGRESS 2015. May 19–22, 2015, Paris, France (poster).

10. F Giardinelli, A Dachille, **F Iacovelli**, E De Cillis, T Acquaviva, G Contegiacomo, AS Bortone. *Mitral chordal rupture: a positioning wires abuse consequence?* Proceedings of the EUROPCR CONGRESS 2015. May 19–22, 2015, Paris, France (clinical case).

11. A Dachille, F Giardinelli, E De Cillis, T Acquaviva, **F Iacovelli**, G Contegiacomo, AS Bortone. *"Protection catheter" in TAVI-related coronary artery dissection.* Proceedings of the EUROPCR CONGRESS 2015. May 19–22, 2015, Paris, France (clinical case).

12. **F Iacovelli**, V Pestrichella, M Cicala, A Pignatelli, T Tesorio, P Rubino, G Contegiacomo. *Percutaneous exclusion of a sinotubular junction pseudoaneurysm using a multi-fenestrated atrial septal defect occluder.* Proceedings of the EUROPCR CONGRESS 2015. May 19–22, 2015, Paris, France (clinical case).

13. A Dachille, N Signore, F Giardinelli, **F Iacovelli**, G Contegiacomo, AS Bortone. *Acute aortic dissection during ineffective attempt of TAVI.* Proceedings of the TCT CONGRESS 2015. October 11–15, 2015, San Francisco, USA (clinical case).

14. A Cioppa, **F Iacovelli**, L Salemme, A Pucciarelli, G Popusoi, S Verdoliva, A Pignatelli, V Pestrichella, G Contegiacomo, AS Bortone, E Stabile, T Tesorio. *Safety and feasibility of single suture-mediated closure system in patients undergoing TAVI with 14-F expandable sheath.* Proceedings of the Leipzig INterventional Course 2016. January 26–29, 2016, Leipzig, Germany (poster).

15. A Cioppa, E Stabile, L Salemme, G Popusoi, A Pucciarelli, S Verdoliva, **F Iacovelli**, A Cafaro, T Tesorio. *Combined use of directional atherectomy and drug coated balloon for the endovascular treatment of common femoral artery disease: one year outcomes of 30 consecutive patients.* Proceedings of the Leipzig INterventional Course 2016. January 26–29, 2016, Leipzig, Germany (poster).

16. F Giardinelli, A Dachille, E De Cillis, T Acquaviva, M Gesualdo, **F Iacovelli**, MM Ciccone, AS Bortone. *IVUS: a way to prevent acute kidney injury in patients undergoing TAVI?* Proceedings of the EUROPCR CONGRESS 2016. May 17–20, 2016, Paris, France (oral contribution).

17. F Cassano, **F Iacovelli**, L Abbracciavento, L Lassandro Pepe, F Pierri, EV Catania, AM Bolognini, V Russo. *Born under a bad S.T.A.R..* Proceedings of the EUROPCR CONGRESS 2017. May 16–19, 2017, Paris, France (clinical case).

18. **F Iacovelli**, L Abbracciavento, F. Cassano, L Lassandro Pepe, M Ligorio, A D'Alessandro, A Chyurlia, V Russo. *The stenting dilemma.* Proceedings of the EUROPCR CONGRESS 2017. May 16–19, 2017, Paris, France (clinical case).

19. L Abbracciavento, L Lassandro Pepe, F Cassano, **F Iacovelli**, M Suma, F Cazzato, S Di Marino, V Russo. *STEMI and double coronary-ventricle fistula.* Proceedings of the EUROPCR CONGRESS 2017. May 16–19, 2017, Paris, France (clinical case).

20. F Giardinelli, A Dachille, E De Cillis, **F Iacovelli**, T Acquaviva, AS Bortone. *Accuracy of IVUS evaluation for the assessment of native valve measures in patients undergoing TAVI: a single centre experience.* Proceedings of the PCR LONDON VALVES CONGRESS 2017. September 24–26, 2017, London, United Kingdom (oral contribution).

21. M Barbanti, MS Van Mourik, MS Spence, **F Iacovelli**, GL Martinelli, DF Muir, F Saia, AS Bortone, CG Densem, F Van der Kley, J Baan, M Thoenes, CM Lüske, P Bramlage, G Costa, CD Owens, M Vis, C Tamburino. *Feasibility and Safety of Early Discharge after Transfemoral Transcatheter Aortic Valve Implantation: The multicentre European FAST-TAVI Trial.* Proceedings of the PCR LONDON VALVES CONGRESS 2018. September 09–11, 2018, London, United Kingdom (late-breaking trials).

- **ABSTRACTS (NATIONAL CONGRESSES)**

1. **F Iacovelli**, P Scicchitano, D Zanna, D Apruzzi, V Marangelli, S Favale. *Endocardite infettiva emboligena: un quadro clinico d'altri tempi*. Proceedings of the 43RD ANMCO NATIONAL CONGRESS. May 30 – June 02, 2012, Florence, Italy (poster). G ITAL CARDIOL. 2012;13(5 Suppl 2):97S

2. **F Iacovelli**, P Scicchitano, L Compostella, N Russo, P Guida, T Setzu, F Bellotto, S Favale. *Miglioramento della funzione endoteliale post-riabilitazione cardiologica.* Proceedings of the 73RD SIC NATIONAL CONGRESS. December 15–17, 2012, Rome, Italy (oral contribution)

3. C Cicala, **F Iacovelli**, A Pignatelli, M Basile, F Masi, D Quagliara, S Favale. *Angina pectoris nel peripartum: quando una coronarografia?* Proceedings of the 73RD SIC NATIONAL CONGRESS. December 15–17, 2012, Rome, Italy (poster)

4. A Pignatelli, **F Iacovelli**, M Basile, C Cicala, C Caiati, D Quagliara, F Masi, S Favale. *Valutazione morfofunzionale complessa in un caso di stenosi coronarica intermedia associata a fistola coronaro-polmonare.* Proceedings of the 73RD SIC NATIONAL CONGRESS. December 15–17, 2012, Rome, Italy (poster)

5. P Scicchitano, **F Iacovelli**, L Compostella, N Russo, P Guida, T Setzu, F Bellotto, S Favale. *Funzione endoteliale ed insulino-resistenza: il ruolo della riabilitazione cardiologica.* Proceedings of the 73RD SIC NATIONAL CONGRESS. December 15–17, 2012, Rome, Italy (poster)

6. **F Iacovelli**, A Pignatelli, Z Palamà, M Basile, C Cicala, V Marangelli, D Quagliara, F Masi, S Favale. *Associazione di coartazione, kinking ed insufficienza aortica: solo un caso?* Proceedings of the 73RD SIC NATIONAL CONGRESS. December 15–17, 2012, Rome, Italy (e-abstract)

7. N Russo, L Compostella, E Vettore, T Setzu, P Scicchitano, **F Iacovelli**, C Bilato, G Tarantini, L Cacciavillani, S Iliceto, F Bellotto. *Comprehensive Cardiac Rehabilitation immediately after an Acute Myocardial Infarction in High Risk Patients: Impact on Prognosis.* Proceedings of the XI SIPREC CONGRESS. March 14–16, 2013, Naples, Italy (poster). HIGH BLOOD PRESS CARDIOVASC PREV 2013; 20(2):107-8

8. M Cicala, **F Iacovelli**, G Balducci, SG Primitivo, V Pestrichella, G Contegiacomo. *"Intention-to-crush" floating struts in the left main.* Proceedings of the 34TH GISE NATIONAL CONGRESS. October 9–11, 2013, Genoa, Italy (oral contribution)

9. M Basile, **F Iacovelli**, A Pignatelli, C Cicala, G Luzzi, M Pepe, F Masi, D Quagliara, S Favale. *Un caso di "recesso intramurale ventricolare" post-estrazione di elettrocatetere.* Proceedings of the 34TH GISE NATIONAL CONGRESS. October 9–11, 2013, Genoa, Italy (poster)

10. G Malerba, **F Iacovelli**, MC Mascolo, M Zingaro, F Masi, D Quagliara, M Pepe, G Luzzi, S Favale. *Riscontro di ematoma intramurale post-estrattivo tramite fistola coronaro-ventricolare.* Proceedings of the 74TH SIC NATIONAL CONGRESS. December 14–16, 2013, Rome, Italy (poster)

11. N Russo, S Ferretto, L Compostella, T Setzu, F Zilio, E Vettore, P Scicchitano, **F Iacovelli**, M Perazzolo Marra, S Iliceto, F Tona, F Bellotto. *Riabilitazione cardiologica intensiva in pazienti stabili con scompenso cardiaco cronico: sicurezza, efficacia ed impatto sulla prognosi.* Proceedings of the 74TH SIC NATIONAL CONGRESS. December 14–16, 2013, Rome, Italy (poster)

12. SG Primitivo, V Pestrichella, M Cicala, S Giannone, **F Iacovelli**, G Contegiacomo. *Teleangectasia emorragica ereditaria: la giusta metodica di trattamento per ogni presentazione*. Proceedings of the 45TH ANMCO NATIONAL CONGRESS. May 29-31, 2014, Florence, Italy (poster). G ITAL CARDIOL. 2014;15(4 Suppl 2):e101

13. M Basile, S Altomare, A Cafaro, V Paradies, **F Iacovelli**, A Pignatelli, A Marchese, F Masi, D Quagliara, S Favale, M Pepe. *TIMI frame count come alternativa all'IMR nella valutazione funzionale del microcircolo coronarico in pazienti con angina stabile e coronarie angiograficamente normali.* Proceedings of the 35TH GISE NATIONAL CONGRESS. October 14–17, 2014, Genoa, Italy (oral contribution). G ITAL CARDIOL. 2014;15(9 Suppl 1):e12-3

14. **F Iacovelli**, AS Bortone, M Cicala, G Martinelli, A Cotroneo, R Montesanti, R Alemanni, A Pignatelli, SG Primitivo, V Pestrichella, T Acquaviva, E De Cillis, M Cassese, G Contegiacomo. *Il profilo emodinamico delle bioprotesi aortiche nel paziente anziano: TAVI ed Edwards Intuity® a confronto.* Proceedings of the 35TH GISE NATIONAL CONGRESS. October 14–17, 2014, Genoa, Italy (oral contribution). G ITAL CARDIOL. 2014;15(9 Suppl 1):e30

15. V Paradies, M Pepe, A Cafaro, F Masi, M Basile, **F Iacovelli**, D Zanna, G Camarda, D Quagliara, R Guglielmi, S Favale. *Time-related effect of P2Y12 inhibitors pre-treatment in patients with acute ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention.* Proceedings of the 35TH GISE NATIONAL CONGRESS. October 14–17, 2014, Genoa, Italy (oral contribution). G ITAL CARDIOL. 2014;15(9 Suppl 1):e31

16. **F Iacovelli**, M Basile, A Pignatelli, C Cicala, A Cafaro, V Paradies, V Alberotanza, M Pepe, F Masi, D Quagliara, G Contegiacomo, AS Bortone, S Favale. *Un caso suggestivo di anomalia coronarica complessa: GUCH o ventricolo sinistro non compatto?* Proceedings of the 35TH GISE NATIONAL CONGRESS. October 14–17, 2014, Genoa, Italy (poster). G ITAL CARDIOL. 2014;15(9 Suppl 1):e46

17. A Pignatelli, V Pestrichella, **F Iacovelli**, M Cicala, SG Primitivo, V Alberotanza, C Larosa, G Minervini, D Manfredi, G Valenti, F Bartolomucci, G Contegiacomo. *Caso complesso di pseudoaneurisma coronarico secondario a dissezione cronica post-PCI.* Proceedings of the 35TH GISE NATIONAL CONGRESS. October 14–17, 2014, Genoa, Italy (poster). G ITAL CARDIOL. 2014;15(9 Suppl 1):e52-3

18. M Cicala, **F Iacovelli**, V Alberotanza, SG Primitivo, V Pestrichella, M Cassese, G Contegiacomo. *Utilizzo di sistema di assistenza cardio-polmonare ECMO durante TAVI trans-femorale.*

Proceedings of the 35TH GISE NATIONAL CONGRESS. October 14–17, 2014, Genoa, Italy (poster). G ITAL CARDIOL. 2014;15(9 Suppl 1):e63

19. **F Iacovelli**, V Pestrichella, M Cicala, SG Primitivo, V Alberotanza, M Cassese, G Contegiacomo. *Esclusione di pseudoaneurisma della giunzione seno-tubulare mediante dispositivo da difetto interatriale multifenestrato.* Proceedings of the 35TH GISE NATIONAL CONGRESS. October 14–17, 2014, Genoa, Italy (poster). G ITAL CARDIOL. 2014;15(9 Suppl 1):e75-6

20. M Cicala, **F Iacovelli**, V Alberotanza, SG Primitivo, V Pestrichella, D Serena, G Contegiacomo. *Esclusione di voluminoso pseudoaneurisma dell'arteria succlavia mediante impianto di stent ricoperti.* Proceedings of the 35TH GISE NATIONAL CONGRESS. October 14–17, 2014, Genoa, Italy (poster). G ITAL CARDIOL. 2014;15(9 Suppl 1):e76

21. G Ricci, **F Iacovelli**, A Cafaro, V Paradies, V Alberotanza, D Zanna, M Pepe, F Masi, D Quagliara, G Contegiacomo, AS Bortone, S Favale, MM Ciccone. *Un caso suggestivo di anomalia coronarica complessa: GUCH o ventricolo sinistro non compatto?* Proceedings of the 75TH SIC NATIONAL CONGRESS. December 13–15, 2014, Rome, Italy (poster)

22. C Caiati, ME Lepera, D Grande, D Santoro, **F Iacovelli**, P Pollice, F Masi, S Favale. *Transthoracic enhanced Doppler echocardiography in convergent color Doppler mode in assessing the physiologic significance of intermediate severity coronary lesions. Validation versus fractional flow reserve*. Proceedings of the 75TH SIC NATIONAL CONGRESS. December 13–15, 2014, Rome, Italy (poster)

23. C Caiati, ME Lepera, P Marolla, D Santoro, A Tito, M Fracchiolla, M Stufano, D Grande, A De Santis, **F Iacovelli**, S Favale. *Atherosclerosis in the left anterior descending coronary artery as assessed by transthoracic enhanced Doppler echocardiography rules out critical right and/or circumflex coronary artery disease.* Proceedings of the 75TH SIC NATIONAL CONGRESS. December 13–15, 2014, Rome, Italy (poster)

24. D Santoro, C Caiati, ME Lepera, D Grande, A Tito, M Stufano, P Marolla, A De Santis, **F Iacovelli**, S Favale. *Transthoracic enhanced coronary echo Doppler in convergent color Doppler mode can distinguish ischemic from non-ischemic left bundle branch block.* Proceedings of the 75TH SIC NATIONAL CONGRESS. December 13–15, 2014, Rome, Italy (poster)

25. **F Iacovelli**, A Pucciarelli, S Verdoliva, L Salemme, A Cioppa, G Popusoi, E Stabile, T Tesorio. *Impatto della gestione laboratoristica sul rischio di insufficienza renale acuta in pazienti*

sottoposti a TAVI. Proceedings of the 46TH ANMCO NATIONAL CONGRESS. June 04-06, 2015, Milan, Italy (oral contribution). G ITAL CARDIOL. 2015;16(5 Suppl 1):e36

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- **COINVESTIGATORSHIPS IN MULTICENTRIC CLINICAL STUDIES:**
  - *FAST-TAVI* (Feasibility and Safety of early discharge after Transfemoral Transcatheter Aortic Valve Implantation)
  - *EuRECS-TAVI* (European Registry on Emergent Cardiac Surgery during TAVI)
  - *INCANTA* (SICI-GISE commuNity CAmpania survey doNna TAVI)
  - *ERIS* (Evolving Routine Standards of FFR Use): studio osservazionale finalizzato a descrivere l'uso corrente nei laboratori di interventistica cardiologica italiani della Fractional Flow Reserve
- **REVIEWERSHIPS:**
  - North American Journal of Medical Sciences (2013)
  - Medical Devices: Evidence and Research (2014)
  - CardioVascular and Interventional Radiology (since 2014)
  - International Journal of Cardiology (2016)
- **EDITORIAL BOARD MEMBERSHIPS:**
  - Journal of Acute Disease (since 2015 to 2017)

Congress partecipation

- **AS INVITED RELATOR:**
  - 25TH SPIGC NATIONAL CONGRESS. June 13–15, 2013, Bari, Italy
  - IFR: EVOLUZIONE DELLA FFR. September 15, 2017, Bari, Italy
- **AS INVITED DISCUSSANT:**
  - CARDIOMONOPOLI 2017. April 28–29, 2017, Monopoli, Italy
  - 39TH GISE NATIONAL CONGRESS. October 16–19, 2018, Milan, Italy
  - SICI-GISE CAMPANIA REGIONAL CONGRESS 2019. April 05–06, 2019, Caserta, Italy

Memberships

- **ITALIAN SOCIETY OF INVASIVE CARDIOLOGY**, since 2016
- **EUROPEAN ASSOCIATION OF PERCUTANEOUS CARDIOVASCULAR INTERVENTIONS**, since 2018

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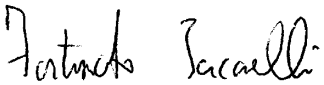
Bari, 05/06/2019

Fortunato Iacovelli



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Acknowledgments

"Truth is found neither in the thesis nor the antithesis, but in an emergent synthesis wich reconciles the two"

Georg Wilhelm Friedrich Hegel

Once I started my PhD I was working as cardiologist at Imperia public Hospital, but after a very short time I moved to Taranto in order to work as intervtionalist. First of all I have to thank Dr. Vitantonio Russo, the head of the division of cardiology of the "SS. Annunziata" Hospital of Taranto, who believed in my research program allowing me to spend about a week per month at the interventional cardiology service of the "Montevergine" clinic of Mercogliano (AV) to carry on some research projects already started under the supervision of Dr. Tullio Tesorio and Prof. Eugenio Stabile. As a fundamental rule of the International PhD, after such two italian research years at Mercogliano, I spent almost all of my last PhD year abroad. I have to thank one again Dr. Vitantonio Russo as well as all the management staff of the A.S.L. Taranto who gave me the possibility to spend such year abroad keeping my interventionalist position in Italy. Particularly I had the pleasure to stay at the Inselspital of Bern, under supervision of Prof. Marco Valgimigli, who gave me fundamental teaching in research, although I have really a lot to learn yet. Once back in Italy,

working at the Policlinico University Hospital of Bari, my research collaboration with Prof. Valgimigli is still continuing and I am confident it will give very good results also in the future.

In all the learning curves as well as the teaching processes, the common habit is to procede ***from simplest to most complex***.

Nevertheless medicine is not an exact science and consequently who could state if something is simpler than something else? In the recent periods, research in interventional cardiology is increasingly driven by commercial interests connected to new devices and drugs' performances. Anyway an opposite pathway could be interesting and didactic at the same time. After analyzing the several complications of last generation structural and peripheral interventional procedures, researching about "normal" coronary arteries sizing has been an essential step of my PhD research pathway. Also if apparently this topic looks empiric, its clinical implications are numerous: the definition of normality will imply a more precise definition of coronary ectasia, and consequently a better knowledge of this disease. Such standardization will be the first stone to lay in order to identify the correct interventional or pharmacological treatment of this not so uncommon coronary disease.