

Title: “Correlation between complete coronary revascularization and both systolic cardiac functions and wall motion score index”.

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Abstract

Objectives: over the past two decades, we have not insisted on complete revascularization. Current study aims to evaluate outcomes after complete coronary revascularization and correlate outcomes with systolic left ventricular functions.

Methods: Between May 2023 and June 2024, for this prospective cohort study, we received fifty-patients with ischemic hypokinetic one or more left ventricular segments, (group-1) and fifty-others with akinetic segments and reduced segmental wall thickness (group-2). Complete coronary re-vascularization was performed for all. They had preoperative and one-year postoperative echo-cardiography, Cardiac magnetic resonance-imaging and angiography plus echocardiography at discharge & one month later.

Results: There were statistically significant differences between study groups regarding age and distribution of the degrees of stenosis. Age showed significant negative inverse correlation with preoperative systolic left ventricular functions. The degree of stenosis showed significant direct positive correlation with age, wall motion score and score index.

Half of the patients in group-1 had 75-90% stenosis, whereas more than half in group-2 had complete occlusions. Left ventricular systolic functions showed statistically significant differences between the measurements done at the 3-time points during the study within both groups and between both groups.

Significant direct positive correlation coefficient between ejection fraction and mitral annular plane excursion-measurements. Significant negative inverse correlation between ejection fraction and wall motion score and score index measurements. There was a weak correlation between wall motion score and ejection fraction measurements.

Conclusions: Complete revascularization is recommended. It reverses ischemic myocardial changes over several months, evidenced by significant improvement in cardiac systolic functions with time.

Registration:

This study was approved and registered by the Research and Research ethical Committee in Faculty of Medicine, Suez Canal University. The Number for registration is (4472 / 11/02/2021). This panel includes authors and Statesian, based on their expertise in the development of clinical practice documents, is trying to establish a uniform methodology for joint society' s projects. The writing panel collaborated to draft all document sections that were reviewed and discussed during several committee meetings. Consensus was achieved in every phase throughout the development process of this study.

Key words: complete coronary revascularization,

coronary artery disease,

wall motion abnormality score-index,

revascularization and systolic let ventricular functions.

Introduction

Complete revascularization: is defined as successful revascularization of all coronary lesions or segments >1.5 mm in diameter with > 50% arterial diameter stenosis [1].

Angiography-based assessment remains the standard of care [2]

Anatomic revascularization may be declared complete if all stenotic vessels are revascularized, irrespective of size and territory supplied; other investigators impose minimum diameter criteria, whereas other researchers differentiate between main vessels and branch vessels [3].

Thus, complete anatomic revascularization:

- Unconditional: All stenotic vessels are revascularized, irrespective of size and territory supplied.
- Conditional: All stenotic vessels greater than a defined diameter are revascularized, all stenotic main-branch vessels are revascularized, irrespective of myocardial viability.

Complete functional revascularization: All ischemic myocardial territories are re-perfused; areas of old infarction with no viable myocardium are not required to be re-perfused.

Complete numeric revascularization: The number of stenotic vessels must equal the number of distal anastomoses [3]. It is to count the number of vessels with stenoses and then to count the number of distal anastomoses (an equal number would be declared a complete numeric revascularization

Current imaging modalities (echocardiography and CMRI) are widely used. Further trials using contemporary methods are warranted to further clarify the impact of viability assessment on patient management, and the cumulative risk of morbidity and mortality. Left ventricular ejection fraction (LVEF) is an important indicator of systolic left ventricular function and of the severity and prognosis of ischemic heart disease. Assessment of regional function using the wall motion score index (WMSI) is an alternative means of evaluating left ventricular function.

Coronary artery calcification is a marker of plaque development and provides direct evidence of the extent of coronary artery disease burden, and predicting future cardiovascular events [4]

Multivessel coronary artery disease presents a clinical challenge in management and decision making. Guidelines provide some reference points, but some areas of uncertainty remain such as the strategy for intermediate stenotic artery lesions. The aim of current study is to correlate between complete revascularization and left ventricular systolic functions before and after surgery.

Methods:

This prospective Cohort study included 100 patients.

They had Off -Pump complete coronary artery revascularization, we used bilateral skeletonized internal mammary arteries as grafts. Also, endoscopically harvested long saphenous vein grafts were applied. We found that the total number of stenoses equal to the number of distal anastomoses (Complete numeric revascularization).

The concomitant presence of myocardial necrosis with myocardial ischemia, stunning or hibernating myocardium may complicate appraisal of left ventricular (LV) function. Several imaging modalities have been proposed for the accurate assessment of myocardial necrosis, viability, and stunning. We applied repeated echocardiography and cardiac magnetic resonance imaging (cardiac MRI) to assess left ventricular functions.

The left ventricle is divided as follows: basal segments, mid segments and apical segments.

Each segment is then scored, using the following criteria:

- (1 point) Normo-kinesia: normal wall thickening and endocardial excursion
- (2 points) Hypokinesia: reduced wall thickening, reduced endocardial excursion
- (3 points) Akinesia: absence of either wall thickening or endocardial excursion
- (4 points) Dyskinesia: systolic outward stretching or thinning. It includes "aneurysmal" wall motion, which bulges eccentrically during both systole and diastole [1].

The wall motion score index is calculated by dividing the sum of the segmental values by the number of myocardial segments (16). A WMSI of 1.0 (16/16) is considered normo-kinetic and correlates with a CMRI calculated ejection fraction of 64%, whereas a WMSI of 3.0 correlates with an ejection fraction of 12% and is considered akinetic. WMSIs of 1.5, 2.0, and 2.5 are designated mild hypokinesia, hypokinesia, and severe hypokinesia respectively

WMSI is a superior predictor of 12-month mortality over LVEF in STEMI patients treated with primary PCI. When examined in multivariable predictive models, WMSI and LVEF perform very well at predicting 12-month mortality [2,3].

Sample Size: calculated according to the equation:

$$N = 2 \{ (Z_{\alpha/2} + Z_B) \times a \}^2 / (U_1 - U_2)^2 \quad (\text{Dawson \& Trapp., 2004}) - [4]$$

So, the sample size will be 100 patients after adding 10% drop-out population in a year.

Inclusion criteria: Multivessel coronary artery disease, hemodynamically stable patients who are candidates for complete conditional anatomic and numeric revascularization, men or women and age below 70 years.

Exclusion criteria:

1 - Hemodynamically unstable patients

2- Cardiogenic shock

3- Complications such as aneurysm score (wall motion score 4),

4- moderate to severe or severe mitral regurgitation or ischemic interventricular septal defect.

5-Severely calcified lesions.

6- Associating valvular severe lesions or lesions indicating cardiac surgical procedures other than CABG.

7- Conduction of cardiac action potential- abnormalities that may result in dyssynchronous contraction, simulating a true decrease in the contractile function of the myocardium , left bundle branch block.

They had preoperative and one-year postoperative echocardiography, Cardiac MRI and angiography. Also, they had echocardiography on discharge & one month later.

Each patient had complete Conditional anatomical, numeric revascularization with on-pump CABG: 176 stenotic lesions (group1) and 180 severe stenoses and occlusive lesions (in group2) which indicated 356 distal anastomoses.

The Data Availability Statement

Data Available on Request: the data underlying this article will be shared at a reasonable request to the corresponding author.

Statistical Section:

We used the mean values and the standard deviation and estimated the P value

Also, the correlation coefficient for different variables in both groups 1 & 2 and the correlation coefficient for preoperative and postoperative data.

The correlation coefficient is a statistical measure of the strength of a linear relationship between two variables. Its values can range from -1 to 1. A correlation coefficient of -1 describes a perfect negative, or inverse, correlation, with values in one series rising as those in the other decline, and vice versa. A coefficient of 1 shows a perfect positive correlation, or a direct relationship. A correlation coefficient of 0 means there is no linear relationship. Correlation coefficients are used to assess the strength of associations between data variables. The “Pearson correlation coefficient,” measures the strength and direction of a linear relationship between two variables. Values always range from -1 for a perfectly inverse, or negative, relationship to 1 for a perfectly positive correlation. Values at or close to zero indicate no linear relationship or a very weak correlation. The coefficient values required to signal a meaningful association depend on the application. The statistical significance of a correlation can be calculated from the correlation coefficient and the number of data points in the sample, assuming a normal population distribution.

To calculate the Pearson correlation, start by determining each variable’s standard deviation as well as the covariance between them. The correlation coefficient is covariance divided by the product of the two variables’ standard deviations.

$$P_{xy} = \text{Cov}(x, y) / \sigma_x \sigma_y$$

where::

ρ_{xy} =Pearson product-moment correlation coefficient (x, y) = covariance of variables x and y

σ_x =standard deviation of x σ_y =standard deviation of y

$\rho_{xy} = \sigma_x \sigma_y \text{Cov}(x, y)$ **where:**

ρ_{xy} =Pearson product moment correlation coefficient $\text{Cov}(x, y)$ =covariance of variables x and y ,

σ_x =standard deviation of x,

σ_y =standard deviation of y . [5]

Ethical considerations: This study was approved by the Research and Research ethical Committee in Faculty of Medicine, Suez Canal University. The Number for registration is (4472 / 11/02/2021). This panel including authors and Statesian, based on their expertise in the development of clinical practice documents, is trying to establish a uniform methodology for joint society's projects. The writing panel collaborated to draft all document sections that were reviewed and discussed during several committee meetings. Consensus was achieved in every phase throughout the development process of this study [6].

We received written informed consent from each participant. All patients were informed and accepted to participate in this study.

Results

Between May2023 and June 2024, we received fifty-patients with ischemic hypokinetic one or more left ventricular segments, stenotic lesions >50 % reduction in diameter in 176 vessels (group1) and fifty-patients: some with akinetic segments, reduced left ventricular wall thickness and total occlusion in 75 vessels and severe stenotic lesions > 90% in 105 vessels (group2), $P<0.05$) (table1). Off-pump complete re-vascularization was performed for each patient. Bilateral internal mammary arteries and endoscopically harvested long saphenous venous grafts were applied.

The serial left ventricular systolic functions measured preoperatively, one and 12 months postoperatively showed that: There was a statistically significant difference between study groups regarding age (table1). Most of the study's participants in both groups were males. Less than one third of the study population were non-smokers. Most of the study participants had at least one 1st degree relative who had a history of ischemic heart diseases (table 1). There were no statistically significant differences between study groups regarding the status of being diagnosed with diabetes and/or hypertension. It can be noted for both categories that the patients with hypertension were less than the non-diseased in count (table 1).

Most of the study participants in both groups had 3 lesions, with a statistically significant difference between both study groups regarding the count of lesions. Half of the patients in group 1 had 75-90% stenosis, whereas more than half of the patients in group 2 had complete occlusions. There was a statistically significant difference between both study groups regarding the distribution of the degrees of stenosis (table 2). There was a significant difference between study groups regarding the number of distal anastomoses in which there were most patients having 3 distal anastomoses in each study group (table 2).

Regarding ejection fraction: there were statistically significant differences between the measurements of ejection fraction done at the 3 time points in the study within both groups. Moreover, there were statistically significant differences between the study groups regarding each measurement recorded for both studies (table 3).

Regarding mitral annular plane systolic excursion changes in the study population: there were statistically significant differences between the measurements of MAPSE done at the pre-operatively and one-year post-operatively within both groups. Moreover, there were statistically significant differences between both study groups regarding each measurement recorded for both studies (table3). Regarding wall motion score-changes (WMS) in the study population: there were statistically significant differences between the measurements of WMS done at the pre-operatively and one-year post-operatively within both groups. Moreover, there was a statistically significant difference between both study groups regarding only the pre-operative measurement recorded for both groups (table3). Regarding wall motion score index changes in the study population: there were statistically significant differences between the measurements of WMSI done at the pre-operative study and one-year post-operatively within each group. Moreover, there were statistically significant differences between both study groups regarding each measurement recorded at the 3 time points in the study (table 3).

Post-operatively, wound infection was recorded by a few cases in both study groups. Myocardial infarction occurred in one case of group 1 and 2 cases of group 2. Mortality was recorded in group 2 for 3 cases, with no statistically significant difference between both study groups regarding wound infection, post-operatively occurring myocardial infarction and mortality (tables 4). Preoperative and postoperative Echocardiographic and Cardiac MRI -data correlation coefficient: A coefficient of 1 shows a perfect positive correlation, or a direct relationship. Values in our results range from -1 for a perfectly inverse, or negative, relationship to 1 for a perfectly positive correlation. Values at or close to zero indicate no linear relationship or a very weak or a non-significant correlation (tables 5,6). Significant direct positive correlation coefficient between ejection fraction and mitral annular plane excursion-measurements. Significant negative invers correlation relationship between age and EF and wall motion score and score index measurements. Weak non-significant correlation coefficient between preoperative MAPSE and one -year EF.as well as the wall motion score and wall motion score index at one-year postoperative measurements also between both preoperative and One-year postoperative data. A positive family history correlates positively with the severity of CAD and number of lesions.

Discussion

Myocardial infarction is the death of cardiac muscles due to prolonged severe ischemia. The pathophysiologic steps include coronary artery occlusion leading to myocardial ischemia due to which myocardial contractility ceases.

Macroscopic changes appear only after 12 hours showing characteristic dark mottling.

Microscopic changes take 6 to 12 hours to develop with the first apparent change being coagulative necrosis. Followed by neutrophilic influx in around 12 to 24 hours.

Loss of nuclei occurs from the 1st to the 3rd day, phagocytosis by macrophages from the 3rd to the 7th day, and granulation tissue formation at the margins. The complete scar takes around 2 months to form.

The ultrastructural changes of reversible ischemia disappear after 5 minutes of reperfusion except for rare, disrupted mitochondria. The swollen mitochondria observed during the first minutes of reperfusion return to control volume, and the myofibrils become contracted rather than stretched.

Thus, the primary goal is to manage myocardial ischemia as early as possible. The earliest preventive approach is to revascularize stenotic lesions as early as reduction in diameter of the coronary artery >50 % to prevent myocardial infarction

There is growing evidence in support of coronary complete revascularization [7].

Complete coronary revascularization may be categorized as anatomic (revascularization of all lesions of at least 50% or 70% in vessels of at least 1.5 or 2 mm in diameter) or functional (revascularization of all ischemia-producing lesions). The beneficial effect of complete revascularization on clinical outcomes has been shown in a randomized trial of patients with ST-segment elevation myocardial infarction: complete anatomic revascularization lowered the incidence of adverse cardiovascular events compared with culprit vessel-only revascularization [8]. The anatomic definition of complete revascularization (CR) that defines territories at risk as those with an angiographic definition of significant obstruction.² Although a functional definition also exists, researchers did not find evidence-based substantial differences between anatomic and functional complete revascularization [9-10]. Others, however, found differences only in those receiving functional revascularizations such as the 2021 study by Veiga Oliveira et al, which directly compared definitions and outcomes in the same cohort of patients and reported only an advantage to functional revascularization (Hazard Risk 0.47, 95% CI 0.23 to 0.97, p = 0.041), [11]. They reported that: complete surgical revascularization has different definitions but with the same impact. We got comparable results when we applied complete conditional anatomical, numeric revascularization with Off-pump CABG. We excluded cases with left ventricular dyskinesia [12]. Dyskinesia score is (4 points) including systolic outward stretching or thinning. It includes "aneurysmal" wall motion, which bulges eccentrically during both systole and diastole [1]. In a clinical trial cohort of 1,147 patients who underwent CABG, 810 (70.6%) received complete revascularization (CR). The primary outcome was a composite of major adverse cardiac events (MACEs), including death from any cause, nonfatal myocardial infarction, or repeat revascularization over a median 4.7 years of follow-up. MACE occurred in 175 patients (21.6%) in the CR group and 86 patients (25.5%) in the incomplete revascularization (IR) group (hazard ratio [HR] 0.87, 95% confidence interval [CI] 0.67 to 1.13, p = 0.29). A total of 97 patients (12.0%) in the CR group and 48 patients (14.2%) in the IR group died (HR 0.93, 95% CI 0.65 to 1.32, p = 0.67); nonfatal myocardial infarction occurred in 49 patients (6.0%) in the CR group and 30 patients (8.9%) in the IR group (HR 0.76, 95% CI 0.48 to 1.2, p = 0.24), and repeat revascularization occurred in 62 patients (7.7%) in the CR group and 39

patients (11.6%) in the IR group (HR 0.64; 95% CI 0.42 to 0.95, p = 0.027) [13]. Authors in the REGROUP trial concluded that in patients with a great burden of co-morbidities who underwent CABG in the REGROUP trial over a median follow-up period of 4.7 years, CR was associated with similar MACE rates but a reduced risk of repeat revascularization [14].

Complete revascularization was superior to culprit-only revascularization. Complete revascularization was associated with a reduction in cardiovascular death or myocardial infarction. Complete revascularization also improved patient-reported health status. This was accomplished without an increase in major bleeding or contrast-induced nephropathy [15].

We are reporting similar mortality and morbidity after complete revascularization as one-year outcome. Mortality and morbidity showed non-significant differences between our groups. Age showed significant negative inverse correlation relationship with left ventricular functions in these patients with coronary artery disease. Age is a non-modifiable risk factor in the progress of atherosclerosis. CAD prevalence increases after 35 years of age in both men and women. A positive family history correlates positively with the severity of coronary artery stenosis and number of lesions. A positive family history is a significant risk factor in the initiation of atherosclerosis. Patients with a family history of premature cardiac disease younger than 50 years of age have an increased CAD mortality risk [16]. There was weak correlation between wall motion score-one year after revascularization and the ejection fraction at the three times of examination. Ejection fraction correlates well with left ventricular wall motion score index.

Limits:

Limited follow up period.

One year follow up is not enough. We may continue this study with the same patients. They will have serial six months-echocardiography and Cardiac MRI.

Conclusion:

Ischemic changes involving the myocardium take a relatively long time, maybe several weeks, before becoming irreversible. Complete surgical revascularization is highly recommended as it reverses ischemic myocardial changes over several months; This is evidenced by progressive improvement in systolic left ventricular functions and wall motion score and score indices over time.

Table 1: Characteristic features for both groups

Table 1 : is showing age, social and medical distribution of study population				
Variable		group 1	group 2	p-value
Age (years)- Mean ± SD		49.22 ± 4.47	53.1 ± 5.88	0.001*
Variable	Attribute	n (%)	n (%)	
Gender	Male	27 (54)	32 (64)	0.309
	Female	23 (46)	18 (36)	
Smoking index	Not smoking	6 (12)	10 (20)	0.065
	<20 pack year	23 (46)	12 (24)	
	20 or more pack year	21 (42)	28 (56)	
Family history	No	10 (20)	7 (14)	0.545
	One person	21 (42)	26 (52)	
	2 people	16 (32)	12 (24)	
	3 people	3 (6)	5 (10)	
Diabetes	No	41 (82)	40 (80)	0.799
	Yes	9 (18)	10 (20)	
Hypertension	No	27 (54)	33 (66)	0.221
	Yes	23 (46)	17 (34)	

*there is statically significant difference

The table above shows that: there is a statistically significant difference between study groups regarding age. There is no statistically significant difference between study groups regarding gender, smoking index, family history of CAD or the status of being diagnosed with diabetes and/or hypertension.

Table 2: Table showing pre-operative vascular properties

Group		1	2	p-value
Variable	Attribute	n (%)	n (%)	
Number of lesions	3	33 (66)	42 (84)	<i>0.038*</i>
	4	17 (34)	8 (16)	
Degree of stenosis	50-74%	4 (8)	0 (0)	<i><0.001*</i>
	75-90%	46 (92)	0 (0)	
	91-99%	0 (0)	21 (42)	
	Complete occlusion	0 (0)	29 (58)	
Number of distal anastomoses	3	33 (66)	44 (88)	<i>0.009*</i>
	4	17 (34)	6 (12)	

*The value is statistically significant,

The number of lesions equals the number of distal anastomoses

Table 3: - Left Ventricular systolic functional changes during the progress of the study

Ejection fraction changes in the study population

Variable	Mean ± SD- Group1	Mean ± SD-group2	p-value
EF - Pre-operative (%)	45.84 ± 0.85	38.98 ± 1.9	<u><0.001</u>
EF - one-month post-operative (%)	54.54 ± 1.53	47.59 ± 2.3	<u><0.001</u>
EF - one-year post-operative (%)	62.29 ± 4.49	70.11 ± 81.58	<u><0.001</u>
Preoperative/postoperative change	<u><0.001</u>	<u><0.001</u>	---

mitral annular plane systolic excursion changes in the study population

Variable	Mean ± SD	Mean ± SD	p-value
MAPSE pre-operative	8.92 ± 0.97	7.08 ± 0.75	<u><0.001</u>
MAPSE - one-year post-operative	12.96 ± 1.03	11.74 ± 1.08	<u><0.001</u>
Pre-post change	<u><0.001</u>	<u><0.001</u>	---

wall motion scores and wall motion score index changes in the study population

Variable	Mean ± SD- group 2	Mean ± SD- group2	p-value
WMS - pre-operative	24.9 ± 1.66	32.38 ± 3.42	<u><0.001</u>
WMS - one-year post-operative	18.44 ± 2.19	19.09 ± 1.92	0.100
Pre-post operative change	<u><0.001</u>	<u><0.001</u>	---
WMSI - Pre-operative	<u>1.73 ± 0.17</u>	<u>2.96 ± 0.62</u>	<0.001
WMSI - one-year	<u>1.13 ± 0.11</u>	<u>1.27 ± 0.07</u>	<0.001

Pre-post change	<u><0.001</u>	<u><0.001</u>	---
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Table 4: is showing post-operative morbidity and mortality:

Group		1	2	p-value
Variable	Attribute	n (%)	n (%)	
Wound infection	No	48 (96)	47 (94)	0.646
	Yes	2 (4)	3 (6)	
MI - one-month	No	49 (98)	48 (96)	0.558
	Yes	1 (2)	2 (4)	
Mortality	No	50 (100)	47 (94)	0.079
	Early	0 (0)	3 (6)	
	Late	0 (0)	0 (0)	

Table 5: Significant Correlations

	Age (years)	EF - Pre-operative (%)	EF - one month (%)	EF - one year (%)	MAPSE pre-operative	MAPSE - one-year	WMS - pre-operative	WMS - one-year	WMSI - Pre-operative	WMSI - one-year	Number of lesions	Degree of stenosis	Number of distal anastomosis/es	Smoking index
EF - Pre-operative (%)	-0.227*													
EF - one month (%)	-0.351*	0.791*												
EF - one year (%)	-0.321*	0.420*	0.506*											
MAPSE pre-operative	-0.215*	0.641*	0.669*	0.156										
MAPSE - one-year	-0.381*	0.403*	0.342*	0.219*	0.511*									
WMS - pre-operative	0.370*	-0.737*	-0.795*	-0.525*	-0.570*	-0.298*								
WMS - one-year	0.127	-0.131	-0.189	0.004	-0.245*	-0.207*	0.165							
WMSI - Pre-operative	0.364*	-0.691*	-0.722*	-0.484*	-0.538*	-0.466*	0.835*	0.226*						
WMSI - one-year	0.255*	-0.480*	-0.563*	-0.515*	-0.401*	-0.168	0.587*	0.07	0.638*					
Number of lesions	-0.034	0.217*	0.201*	0.332*	0.103	0.182	-0.204*	0.01	-0.235*	-0.101				
Degree of stenosis	0.246*	-0.795*	-0.784*	-0.413*	-0.693*	-0.453*	0.801*	0.19	0.756*	0.529*	-0.199*			
Number of distal anastomosis/es	-0.096	0.246*	0.202*	0.311*	0.123	0.235*	-0.221*	0.026	-0.278*	-0.158	0.892*	-0.268*		
Smoking index	-0.056	-0.079	-0.154	0.036	-0.025	0.158	0.067	-0.172	-0.104	-0.143	0.227*	0.038	0.188	
Family history	-0.249*	0.057	-0.078	-0.102	0.009	-0.054	-0.022	0.034	0.071	0.104	0.14	-0.008	0.185	0.122
* Significant														

The table above shows the statistically significant correlations within the study. Correlations which are significant are marked with an asterisk *.

Table 6: preoperative and postoperative Echocardiographic and Cardiac MRI -data correlation coefficient:

	EF - Pre-operative (%)	EF - one month (%)	EF - one year (%)	MAPSE pre-operative	MAPSE - one-year	WMS - pre-operative	WMS - one-year	WMSI - Pre-operative
EF - one month (%)	0.791*							
EF - one year (%)	0.420*	0.506*						
MAPSE pre-operative	0.641*	0.669*	0.156					
MAPSE - one-year	0.403*	0.342*	0.219*	0.511*				
WMS - pre-operative	-0.737*	-0.795*	-0.525*	-0.570*	-0.298*			
WMS - one-year	-0.131	-0.189	0.004	-0.245*	-0.207*	0.165		
WMSI - Pre-operative	-0.691*	-0.722*	-0.484*	-0.538*	-0.466*	0.835*	0.226*	
WMSI - one-year	-0.480*	-0.563*	-0.515*	-0.401*	-0.168	0.587*	0.07	0.638*

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Conflict of interest statement: The authors declare that no conflicts of interest exist.

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