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Incidence of contrast-induced nephropathy in complete versus culprit only revascularization in old patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention

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ABSTRACT

Objectives: To compare complete revascularization with a culprit-only revascularization in patients presenting with ST-segment elevation myocardial infarction (STEMI) and multivessel disease. *Background*: Although several trials have compared complete with culprit-only revascularization in STEMI, it remains unclear whether complete revascularization may lead to improvement in hard endpoints (death, contrast-induced nephropathy and renal hemodialysis). *Methods*: It's a cohort trial, the patients in our study were randomized into 2 groups; one of them had complete revascularization while the other group had culprit-only revascularization. *Results:* Our study including a total of 140 patients. 70 patients had complete revascularization, 65 patients at immediate procedure and 6 patients within 72h from initial procedure. The other 70 patients had only culprit revascularization. The exclusion criteria included patients who had chronic total occlusion (CTO) or creatinine clearance <30ml/min. Compared with a culprit-only strategy, complete revascularization had significantly higher risk for contrast induced nephropathy (CIN) p=0.016 but no significant difference between the two groups regarding renal replacement therapy during hospital stay or within one month p=0.15,p=0.31 respectively. There is also no significant difference between the two groups regarding one month mortality p=0.31. *Conclusions:* culprit-only revascularization reduces the risk of CIN in patients presenting by STEMI but don't differ in incidence of mortality or renal replacement therapy.

Keywords: complete revascularization; culprit; STEMI; Primary PCI; cardiogenic shock

1. BACKGROUND

ST-segment elevation myocardial infarction is responsible for significant morbidity and mortality worldwide. According to the GRACE study, 38% of patients presented with acute coronary syndrome have STEMI (Goodman et al., 2009). Contrast induced nephropathy is a grave complication of angiographic procedures and arises from administration of iodinated contrast media (McCullough et al., 1997; Ramezani et al. 2019). It is the third most common cause of hospital acquired acute renal injury representing about 12% of the cases. The incidence of CIN varies from 0 to 24% depending on the patient's risk factors (Errin et al., 2012). Contrast induced nephropathy is most commonly defined when either of the following occur, within 48-72 hours after contrast administration or cannot be attributed by other causes (Maddox, 2002; Aspelin, 2004). A 25% increase in serum creatinine (SCr) concentration from baseline value, or an absolute increase in SCr of at least 0.5 mg/dL (44.2 μmol/L).

At the current time, there are several randomized controlled trials examining the effect of non-culprit vessel PCIat time of primarypercutaneous Coronary Intervention (PPCI) (Juan et al., 2018). So in general, three PCI strategies can be identified: Culprit vessel-only PPCI with and PCI of the non-culprit arteries only for spontaneous angina or myocardial ischemia on stress testing; MV PCI at the time of PPCI, guided by angiography or fractional flow reserve (FFR); Culprit vessel-only PPCI, followed by angiography or FFR-driven staged PCI of non-culprit arteries during the index hospitalization or after hospital discharge.

2. METHODOLOGY

This a prospective cohort study concluded 140 patients ≥ 60 years who presented by STEMI & multi vessel disease and underwent primary PCI in primary care center in Cairo from 1-2-2018 till 31-12-2019.

Study population

Inclusion criteria

Patients (≥ 60 years old) who will present with STEMI in primary care centers in Cairo undergoing primary PCI.

STEMI is a clinical syndrome defined by characteristic symptoms of myocardial ischemia in association with persistent electrocardiographic (ECG) ST elevation and subsequent release of biomarkers of myocardial necrosis (Hwang, 2014).

Exclusion criteria

- Patients with known severe reduction in GFR Creatinine clearance <30ml/min
- Patient with CTO of epicardial vessels

Study tools and procedures

- On patients' admission basic clinical data will be obtained.
- Age & sex
- Smoking status

A-Physical examination: including general & local examination with proper assessment of initial Killip of the patient. 12 lead ECG at the time of admission: Diagnostic ST elevation in the absence of left ventricular (LV) hypertrophy or left bundle-branch block (LBBB) is defined as new ST elevation at the J point in at least 2 contiguous leads of ≥2 mm (0.2 mV) in men or ≥1.5 mm (0.15 mV) in women in leads V2–V3 and/or of ≥1 mm (0.1 mV) in other contiguous chest leads or the limb leads (Hwang, 2014).

B-Medical history including: Hypertension ;defined as a systolic blood pressure of 140 mm Hg or more, or a diastolic blood pressure of 90 mm Hg or more, or taking antihypertensive medication (Sun et al., 2014). Diabetes mellitus (DM); which is diagnosed, according to American Diabetes Association, based on a fasting plasma glucose ≥126 mg/dl, a random plasma glucose ≥200 mg/dl plus associated symptoms of hyperglycemia or a HbA1c level ≥6.5 % (American Diabetes, 2020). *Dyslipidemia,* defined according to ESC guidelines as total cholesterol ≥200 mg/dl, Triglyceride level >150 mg/d, LDL ≥100 mg/dl, or patient on lipid lowering drugs (Catapano et al., 2016). Chronic kidney disease (CKD), defined as either kidney damage or a decreased glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m^2 for at least 3 months (Schnaper, 2014). Prior PCI, coronary artery bypasses grafting (CABG) or acute coronary syndrome (ACS).

C-Angiographic Data: Data regarding percutaneous Coronary Intervention(PCI) procedure will be obtained regarding number of vessels involved, the target of PCI procedure (the culprit vessel only or other vessels were targeted), the type of intervention performed whether PTCA or stent placement was done. TIMI flow assessment after procedure: TIMI classified to

TIMI 0 (no perfusion): No antegrade flow beyond the point of occlusion.

TIMI 1(penetration without perfusion): The contrast material passes beyond the area of obstruction but "hangs up" and fails to opacify the entire coronary bed distal to the obstruction for the duration of the cine angiographic filming sequence.

TIMI 2(partial perfusion): The contrast material passes across the obstruction and opacifies the coronary bed distal to the obstruction.

However, the rate of entry of contrast material into the vessel distal to the obstruction or its rate of clearance from the distal bed (or both) are perceptibly slower than its entry into or clearance from comparable areas not perfused by the previously occluded vessel - e.g., the opposite coronary artery or the coronary bed proximal to the obstruction.

TIMI 3(complete perfusion): Antegrade flow into the bed distal to the obstruction occurs as promptly as antegrade flow into the bed proximal to the obstruction, and clearance of contrast material from the involved bed as rapid as clearance from an uninvolved bed in the same vessel or the opposite artery (Chesebro, 1987).

D-Laboratory investigations: full labs including on admission serum

E-Echocardiography: during admission to asses left ventricular function and detect any complicationscreatinine level and following up creatinine level at 48 and 72 hours.

F-In-hospital course: we followed patients regarding any complication including CIN, renal replacement therapy and mortality

G-Follow up of the patients for 1 month for possibility of mortality of needing hemodialysis

End Points

Primary end point: contrast induces nephropathy.

Secondary end points: mortality within one month, renal dialysis during hospital stay or within one month, CKMB and EF

3. RESULTS

Baseline demographic and clinical data

The characteristics of demographic and clinical data between patients with complete revascularization (Patient group) and patient with culprit only revascularizations (control group) are shown in Table 1and Table 2, respectively.

Table 1 Demographic and clinical data among the studied patients

		Culprit only group	Total revisualization group	Test value	P-value	Sig.
		No. = 70	No. = 70			
Age	Mean ± SD	63.56 ± 3.72	64.11 ± 5.32	-0.717•	0.474	NS
	Range	60 – 74	60 – 80			
Sex	Male	57 (81.4%)	54 (77.1%)	0.391*	0.532	NS
	Female	13 (18.6%)	16 (22.9%)			

Table 2 Demographic and clinical data among the studied patients

		Culprit only group		Total revascularizations group		Test value*	P-value	Sig.
		No.	%	No.	%			
Smoking	Positive	42	60.0%	42	60.0%	0.000	1.000	NS
	Negative	28	40.0%	28	40.0%			
HTN	Positive	39	55.7%	47	67.1%	1.929	0.165	NS
	Negative	31	44.3%	23	32.9%			
DM	Positive	36	51.4%	37	52.9%	0.029	0.866	NS
	Negative	34	48.6%	33	47.1%			

Dyslipidemia	Positive	42	60.0%	35	50.0%	1.414	0.234	NS
	Negative	28	40.0%	35	50.0%			
CKD	Positive	16	22.9%	14	20.0%	0.170	0.680	NS
	Negative	54	77.1%	56	80.0%			
Prior ACS	Positive	18	25.7%	20	28.6%	0.144	0.704	NS
	Negative	52	74.3%	50	71.4%			
Prior PCI	Positive	6	8.6%	7	10.0%	0.085	0.771	NS
	Negative	64	91.4%	63	90.0%			
Killip	1	63	90.0%	58	82.9%	1.522	0.217	NS
	4	7	10.0%	12	17.1%			

Comparison between two groups regarding dye used, duration of procedure and CIN

There was no significant difference between the two groups regarding the type of dye used in procedure, P=0.1.but there was highly significant difference between two groups regarding amount of dye and duration of the procedure, p=0.000, 0.000 respectively (Table 3).

Table 3 Type & amount of dye, duration of procedure

		Culprit only group	Total revascularizations group	Test value	P-value	Sig.
		No. = 70	No. = 70			
amount of dye (ml)	Mean ± SD	188.00 ± 60.28	245.86 ± 94.14	-4.330•	0.000	HS
	Range	50 – 350	100 – 500			
Type of dye	Ultravist	2 (2.9%)	7 (10.0%)	4.613*	0.100	NS
	Omnipaque	63 (90.0%)	54 (77.1%)			
	Telebrix	5 (7.1%)	9 (12.9%)			
Duration of procedure (min)	Median (IQR)	25 (20 – 30)	45 (35 – 60)	-4.189‡	0.000	HS
	Range	10 – 90	25 – 130			

Primary end point

CIN was significantly higher in patients had complete revascularizations, (p=0.016) Table 4 and Figure 1.

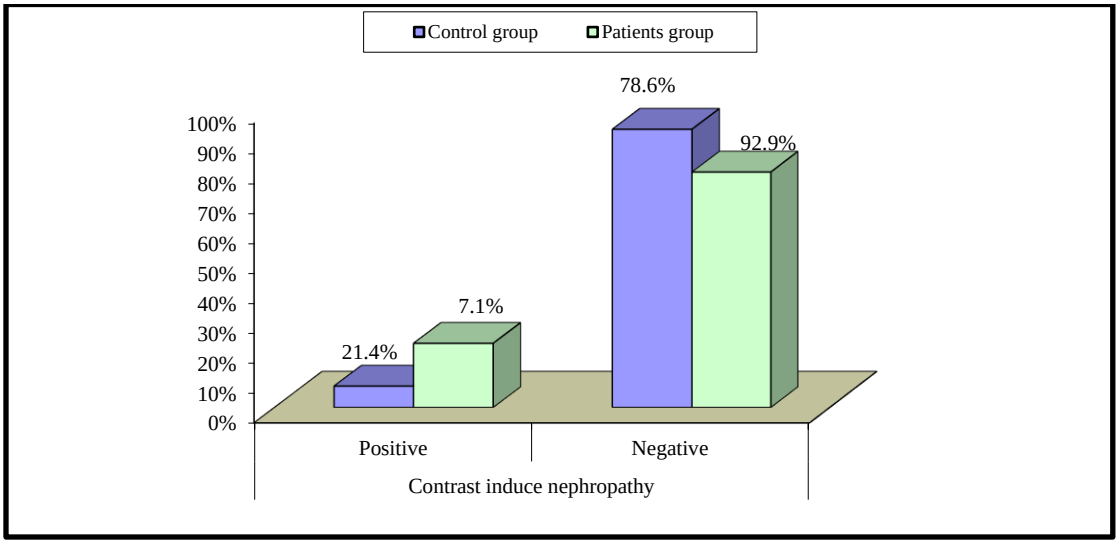

Figure 1 The primary end point (CIN)

Table 4 The primary end point (CIN)

		Culprit only group	Total revascularizations group	Test value	P-value	Sig.
		No. = 70	No. = 70			
Contrast induce nephropathy	Positive	5 (7.1%)	15 (21.4%)	5.833*	0.016	S
	Negative	65 (92.9%)	55 (78.6%)			

Secondary end points

There was no significant difference between the two groups regarding renal dialysis during hospital admission or during one month, (p=0.1, 0.3 respectively) Table 5 and Figure 2. Also there was no significant difference between the two groups regarding one month mortality, (p=0.3) Table 5 and Figure 2. There was no significant difference between two groups regarding EF during admission and CK total peak, (p=0.2, 0.08 respectively) Table 6. The only significant difference between the two groups was CKMB peak which was higher in patients with total revascularizations, (P=0.000) Table 6 and Figure 3.

Table 5 Dialysis and mortality in both groups

		Culprit only group		Total revascularizations group		Test value*	P-value	Sig.
		No.	%	No.	%			
Dialysis during hospital admission	Positive	0	0.0%	2	2.9%	2.029	0.154	NS
	Negative	70	100.0%	68	97.1%			
1 month dialysis	Positive	0	0.0%	1	1.4%	1.007	0.316	NS
	Negative	70	100.0%	69	98.6%			
1 month mortality	Positive	0	0.0%	1	1.4%	1.007	0.316	NS
	Negative	70	100.0%	69	98.6%			

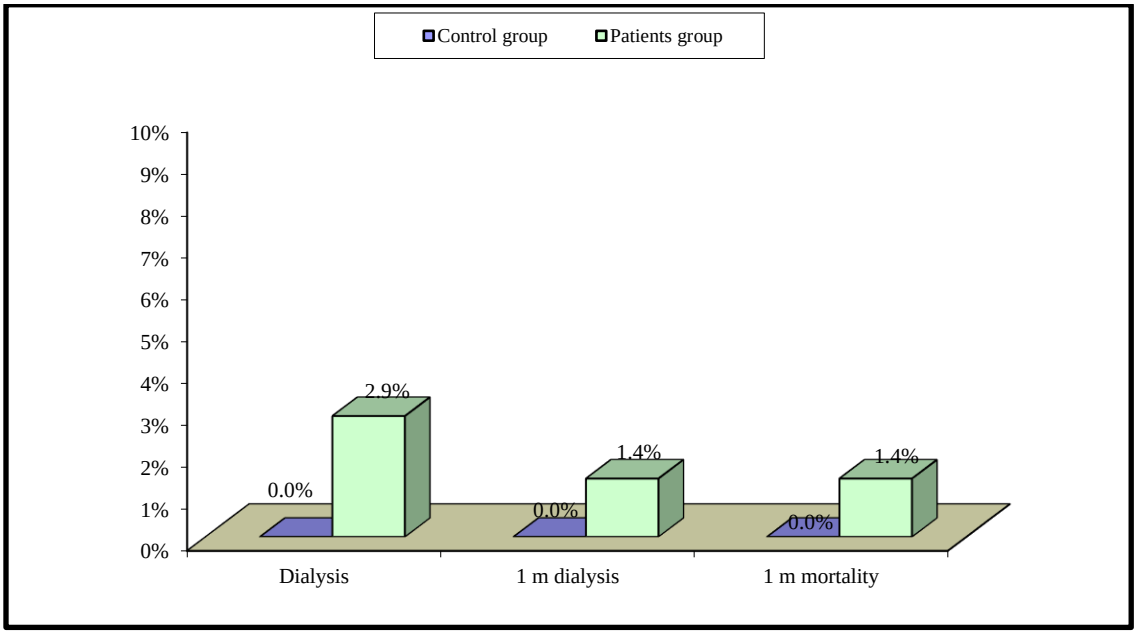

Figure 2 Dialysis and mortality in both groups

Table 6 CK peak and EF

		Culprit only group	Patients group	Test value	P-value	Sig.
		No. = 70	No. = 70			
CKt peak	Median (IQR)	847.5 (600 - 1435)	750 (450 - 1132)	-1.715‡	0.086	NS
	Range	280 – 5105	200 – 6621			
CKMB peak	Median (IQR)	103.5 (72 - 160)	175 (110 – 260)	-3.883‡	0.000	HS

	Range	20 – 599	29 – 695			
EF (%)	Mean ± SD	46.80 ± 6.47	45.34 ± 7.95	1.190•	0.236	NS
	Range	35 – 60	25 – 60			

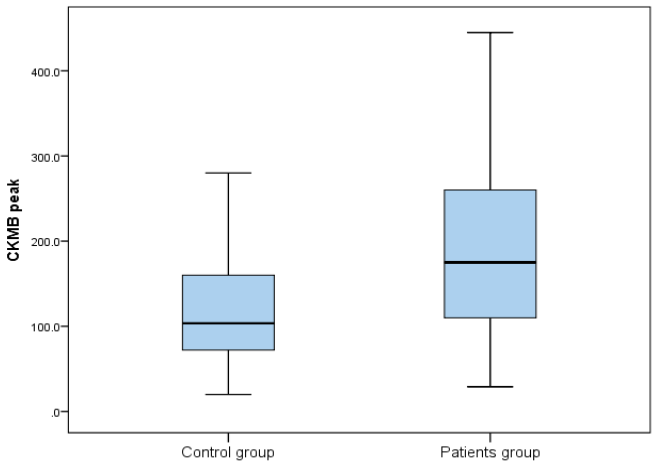

Figure 3 CK MB in both groups

4. DISCUSSION

Our study is discussing one of the most controversial topics in interventional cardiology in patients presenting with STEMI. Up till now many cardiologists are still discussing, during intervention of patients with STEMI and multivessels disease whether they should revascularize the culprit lesion only or it's better to proceed to complete revascularizations. A lot of studies were published discussing this question and had different recommendations. Most of these studies focused on the major adverse cardiac events (MACE), including, cardiac mortality, reinfarction, rePCI with little concern on the effect of the strategy of revascularization on kidney. So in our study we are mainly discussing the effect of the revascularization strategy on incidence of CIN and whether CIN is higher in patients with complete revascularization or patients with culprit only revascularization. We also discuss in our study the effect of revascularizations' strategy on mortality and renal dialysis as secondary end points. In our study we recruited 140 patients ≥ 60 years who presented by STEMI & multi vessel diseases and underwent PPCI in primary care centers in Cairo our patients divided into 2 groups:

Group 1 (70 patients): only culprit lesion PCI was performed at the initial procedure (Control group).

Group 2 (70 patients): Revascularization was done to the culprit lesion and all other non-culprit lesion ≥2mm in major vessel with >70% stenosis (Patients group).

Demographic & clinical data

In comparison of our study demographic data to the complete trial study published on October 2019, we found that our patients had higher prevalence of risk factors especially DM and renal impairment. The demographic data of complete trial was as follows, DM (19.1% in patients had complete revascularizations and 19.9% in patients with culprit only revascularizations. CKD (2% in patients had complete revascularizations and 2.3% in patient had culprit only revascularization. HTN (48.7% in complete revascularizations group and 50.7% in patients had culprit only revascularizations. Prior ACS (7.3% in patient had complete revascularization group and 7.6% in patients had culprit only revascularizations. Prior PCI (7% in both groups) the mean of age and sex were near in our study in comparison to complete trial (mean age was 61.6 in patient had complete revascularization and 62.4 in patients had culprit only revascularizations. Male patients represent 80.5% in group had complete revascularization and 79.1% in patients had culprit only.

Our patients who had Killip class 4 were 17.1 % in complete revascularizations group and 10% in patients had culprit only revascularizations while in complete trial patients with Killip 3 and 4 were 10.9 % in complete revascularizations group and 10.6% in patients had culprit only revascularizations. In comparison to Culprit-Shock trial Prevalence of DM and dyslipidemia was also higher in our population. As in (Culprit-Shock) trial, prevalence of DM was (34.6% in patients had complete revascularizations and

30.3% in patients had culprit only revascularizations. Dyslipidemia was 34.8% in patients had complete revascularizations and 33.1% in patient had culprit only revascularizations.

In Culprit-Shock trial the mean age of study population was higher than our study (mean age 70 years), also had higher prevalence in prior PCI (18.8% and 18.9). 78.1% were males in complete revascularizations group while males represent 74.9% in patients had culprit only revascularizations. Prevalence of prior ACS was lower in populations studied in Culprit-Shock trial. Patients presented by impaired renal perfusion and oliguria were 28.5% in complete revascularizations group and 24% in culprit only revascularizations group.

In our study there was no significant difference between the two groups regarding the culprit vessel and non-culprit vessels, these findings were the same in the Culprit-Shock trial and Complete trial. We concluded that complete revascularizations in patients presented by STEMI increase the incidence of CIN in comparison to patients had culprit only revascularization, P=0.016, but does not significantly increase the need for renal replacement therapy (renal dialysis or ultrafiltration) either during hospital stay or after one month, P=0.15, 0.31. These findings coincide with the results of Culprit-Shock trial. Although the study didn't discuss the incidence of CIN but it studied the incidence of needing renal replacement therapy after 30 days or one year there was no significant difference between patients who had complete revascularizations and patients who had culprit only revascularizations, p=0.07, 0.7 respectively .

Our results are different from that of the complete trial in which complete revascularizations didn't statistically increase the incidence of CIN. This difference between the two studies may be due to different contributing factors, as the mean age of our populations was higher (64.11 ± 5.32 vs 62.4±10.7). The prevalence of our populations' risk factors of CIN like DM, dyslipidemia, HTN, CKD, prior ACS prior PCI were higher in our population. Another remarkably important point causing this difference is the strategy used in intervention, as most of our patients had immediate complete revascularizations during the initial procedure (92%) while in complete trial; complete revascularizations for all cases were done on different stages within 45 days from the initial procedure.

In our study we focused on the effect of amount of dye, duration of procedure on the incidence of CIN and concluded that the higher amount of dye and longer duration of procedure increase the incidence of CIN. The type of dye didn't affect incidence of CIN, most probably because 87% of dye used in patient group, 93% used in control group was from the same type, nonionic low-osmolar dye. This point wasn't discussed in complete trial, but Giancarlo et al. (2009) study the effect of contrast volume on incidence of CIN and agreed with our study that the higher contrast volume the higher rates of CIN. Anthony et al. (2014) study the incidence of CIN in Culprit Trial and concluded that complete revascularizations didn't increase the incidence of CIN but in this study there were only 2 patients in each group who had CIN and the prevalence of risk factors in complete revascularizations group were less than our study (DM 12.9%, HTN 36.6%, dyslipidemia 27.9% prior ACS 4.8%, Prior PCI 4.1% TIMI > 16.8%).

We also concluded that complete revascularizations don't increase incidence of cardiac mortality during hospital stay and after one month of follow up as only one patient having compete revascularizations died and this was not statically significant. This goes with Culprit Trial results, also MACE (all cause mortality, recurrent MI , HF, repeated revascularization) was statistically higher in group who had culprit only revascularization but when comparing mortality cases in both groups there was no significant difference between culprit only and total revascularization, P=0.14 .

On the other hand, Authors of Complete trial concluded that mortality was significantly higher in culprit only revascularizations group, P=0.004, this may be due to larger sample size (4041 patients), longer duration of follow up (3 years) and large age of the study population which may contribute to critical non culprit lesions. Another difference from Culprit-Shock trial, the one-month mortality was significantly higher among patients having total immediate revascularizations, P=0.03. Patients included in this study were shocked and this may explain why this result occurred. Multiple stenting mean longer duration of procedure, larger amount of dye and more organ hypoperfusion injury.

5. CONCLUSION

Patients presenting by STEMI and having complete revascularizations are at higher risk of developing CIN from those having culprit only revascularizations. The strategy of revascularizations either completes revascularizations or culprit only revascularizations didn't affect the incidence of mortality or the need for renal replacement therapy within one month of the procedure.

Abbreviations

ACS	Acute coronary syndrome

CIN	Contrast induced nephropathy
CKD	Chronic kidney disease
CTO	Chronic total occlusion
CABG	Coronary artery bypass grafting
DM	Diabetes mellitus
PCI	Percutaneous coronary intervention
PPCI	Primary Percutaneous coronary intervention
STEMI	ST-segment elevation myocardial infarction

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Author Contributions

Ahmed Behiery collected, analyzed, and interpreted the data and writing the manuscript. Mohamed Zahran revised the data set. Mohamed Atef revised the data set. Nireen Okasha professor of cardiology interpreted the patient's data and was a contributor to writing the manuscript. All authors read and approved the final manuscript.

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Conflict of Interest

The authors declare that there are no conflicts of interests.

Informed consent

Written & Oral informed consent was obtained from all individual participants included in the study.

Ethical approval

The study was approved by the Medical Ethics Committee of Faculty of Medicine, Ainshams University, Cairo (ethical approval code: FMASU MD 77/2018).

Data and materials availability

All data associated with this study are present in the paper.

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