

Gender difference in clinical outcomes of the patients with coronary artery disease after percutaneous coronary intervention

A systematic review and meta-analysis

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Abstract

Background and objectives: Previous researches have reported the controversial results regarding the gender difference in clinical outcomes of patients with coronary artery disease after percutaneous coronary intervention. Hence, this systematic review and meta-analysis was designed to investigate whether gender difference existed in patients with coronary artery disease after percutaneous coronary intervention.

Methods: PubMed, Embase, and the Cochrane Library database were searched up to February 10, 2018. Studies comparing the gender-specific effect on clinical outcomes of patients with coronary artery disease after percutaneous coronary intervention were identified, to analyze mortality, major adverse cardiovascular events (MACE) and revascularization. Statistical software RevMan was utilized in this meta-analysis.

Results: A total of 49 studies, involving 1,032,828 patients (774,115 males and 258,713 females) reporting gender-specific outcomes, were included in this study. The in-hospital mortality, 30-day mortality, 1-year mortality, and at least 2-years mortality in male patients with coronary artery disease after percutaneous coronary intervention were significantly lower than those of females (odds ratio [OR] 0.58 95% confidence interval [CI] 0.52–0.63, $P < .001$; OR 0.64, 95% CI 0.61–0.66, $P = .04$; OR 0.67, 95% CI 0.60–0.75, $P < .001$ and OR 0.71, 95% CI 0.63–0.79, $P = .005$, respectively). The MACE was significantly decreased in male subjects after initial percutaneous coronary intervention compared with females in < 1 -year or at least 1-year (OR 0.67, 95% CI 0.56–0.80, $P < .001$ and OR 0.84, 95% CI 0.76–0.93, $P < .001$). The male patients after percutaneous coronary intervention harbored higher rate of revascularization compared with females for at least 1-year (OR 1.17, 95% CI 1.00–1.36, $P < .001$), while the rate of revascularization in male patients for < 1 -year was lower than that of females (OR 0.93, 95% CI 0.69–1.26, $P < .001$).

Conclusions: The systematic review and meta-analysis suggests that the prognosis of male patients with coronary artery disease after percutaneous coronary intervention is better than that of females, except for long-term revascularization.

Abbreviations: CI = confidence interval, MACE = major adverse cardiovascular events, OR = odds ratio, PCI = percutaneous coronary intervention.

Keywords: coronary artery disease, gender, percutaneous coronary intervention

1. Introduction

Coronary artery disease is the most common cardiovascular disease caused by coronary stenosis, spasm or occlusion. It is estimated that

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up to 23.3 million people will die of cardiovascular disease by 2030.^[1] To improve patient's viability, percutaneous coronary intervention (PCI) is the most commonly applied approach of reperfusion in many countries. However, multiple researches have pointed out that there were some prognostic differences between different genders.^[2–44] Some studies have showed persistent gender difference in outcomes after adjusting multivariate factors,^[2,5,7,9,10,13,15,18,20–25,28,30–33,35–39,41–43] while other studies also demonstrated that gender was not an independent factor for patient's outcome.^[3,4,11,12,14,17,19,26,27,29,34,40,44] Although previous meta-analysis has demonstrated the effect of gender on response to PCI, which not involved major adverse cardiovascular events (MACE) and revascularization, and the follow-up period was also comparatively short.^[45–48] Therefore, this meta-analysis was designed to determine the gender difference in patients with coronary artery disease after PCI, and provide evidence for the development of the guideline.

2. Materials and methods

2.1. Date source and search strategy

PubMed, Embase, and the Cochrane Library database were searched up to February 10, 2018. The following keywords and

medical subject headings were utilized according to the “PICO” strategy: “coronary artery disease”, “percutaneous coronary intervention” or “PCI”, “gender”, or “sex”. Meanwhile, to prevent missing the related articles, the bibliography of the articles included in this study was retrieved manually. All analyses were based on previously published studies, thus no ethical approval and patient consent are required.

2.2. Study selection and quality assessment

Three reviewers (YYG, FHY, and CLF) preliminarily and independently screened the articles that were eligible for study based on the title and summary. In the case of disagreements, the issues were solved through tripartite negotiation when checking the selected articles. The filtered article satisfied the following criteria: Coronary artery disease, including acute coronary syndrome, acute myocardial infarction, ST-segment elevation myocardial infarction, non-ST-segment elevation myocardial infarction, non-ST segment elevation acute coronary syndrome, unstable angina, and stable coronary artery disease; patients undergoing PCI; gender, sex, female, and male; gender-related different outcomes, including short and long-term mortality, MACE, revascularization. In this meta-analysis, all original articles were endeavored to collect, without considering case reports, summaries of the meeting or relevant comments of the original study. The Cochrane collaboration’s tool^[49] and Newcastle–Ottawa scale^[50] were utilized to assess the quality of randomized controlled trials and observational studies.

2.3. Outcome definition

The outcomes of this pooled analysis included 3 primary endpoints, that was, mortality, MACE, and revascularization. The mortality was assessed mainly from in-hospital mortality, 30-day mortality, 1-year mortality, and at least 2-years mortality. The MACE and revascularization were divided by the cutoff of 1 year, including <1-year and at least 1-year MACE, revascularization for <1 year and at least 1 year.

2.4. Statistical analysis

Statistical software RevMan (version 5.3, Cochrane Collaboration Network) was utilized for data analysis in this meta-analysis. For all the outcomes, dichotomous data were pooled as Mantel–Haenszel odds ratio (OR) with the corresponding 95% confidence interval (CI). Statistical heterogeneity was evaluated by Chi-square test, which was showed by I^2 statistic. Fixed effects models were employed in the case of no evidence of heterogeneity ($I^2 \leq 50\%$), otherwise random effects model was used. Subgroup analysis was performed to figure out sources of heterogeneity in the case of large heterogeneity. Sensitivity analysis was performed to determine whether any single study was primarily responsible for the final results. All statistical tests were two-tailed, and a P value < 0.05 was considered as statistical significance.

3. Results

3.1. Search results

A total of 6636 articles were retrieved, of which 157 related articles were identified after screening the title and abstract. Studies with subjects < 100 , non-English literature and those failed to meet the inclusion criteria of the study were excluded by reading the full text. Final only 49 nonrandomized control studies

are included, which 13 studies were from Asian countries, 25 studies from European countries, 11 studies from North American, and 2 studies from Australia. The duration of follow-up varied from hospital stay to 30-day, and lasting to 7 years. The NOS was utilized to evaluate all the enrolled studies in this pooled analysis. Of them the quality score was 7 and 8 in 16 and the remaining 33 studies on the 0 to 10 scoring system, respectively (see Table, Supplemental Content, <http://links.lww.com/MD/C358>, which illustrates the specific scores for each study).

3.2. Baseline data characteristics

Age, a history of hypertension, hyperlipidemia or dyslipidemia, diabetes mellitus, and smoking are reviewed by carefully reading the full text and summarizing the baseline data of each study (Table 1). Meanwhile, the male patients with coronary artery disease after PCI were found to harbor lower incidence of hypertension (OR 0.58, 95% CI 0.47–0.71, $P < .001$), diabetes (OR 0.72, 95% CI 0.68–0.77, $P < .001$), hyperlipidemia or dyslipidemia (OR 0.98, 95% CI 0.94–1.02, $P < .001$), and cardiogenic shock (OR 0.78, 95% CI 0.65–0.92, $P < .001$) compared with females. Although the smoking rate of male subjects (OR 2.65, 95% CI 2.16–3.24, $P < .001$) was higher than that of females, but the symptom onset time, door-to-balloon time and reperfusion time for female patients with coronary artery disease after PCI were longer than those of males (Table 2). In addition, the age of male patients is younger compared with females (Table 1).

3.3. The mortality

The 24 studies (n=430,914)^[5,10,12,14,18,19,21,22,24–28,30,32,35,37,39,40,41,43,44,51,52] reported on PCI postoperative in-hospital mortality, which show that the in-hospital mortality of male patients was significantly lower than that of females (OR 0.58, 95% CI 0.52–0.63, $P < .001$, $I^2 = 66\%$) (Fig. 1). This gender differences also reflect in 30-day mortality [OR 0.64, 95% CI 0.61–0.66, $P = .04$, $I^2 = 40\%$; 19 studies (n=523,304)]^[2–4,7,8,13–17,23,25,26,33–36,42,53] 1-year mortality [OR 0.67, 95% CI 0.60–0.75, $P < .001$, $I^2 = 73\%$; 20 studies (n=590,590)]^[8,10,13,15–17,20,25,26,28,30,33,35,36,38,43,44,53–55] and >2-years mortality [OR 0.71, 95% CI 0.63–0.79, $P = .005$, $I^2 = 57\%$; 14 studies (n=43,096)]^[4–6,18,19,23,29,31,34,36,40,43,52,56] (Figs. 2–4). Due to the low heterogeneity ($I^2 < 50\%$) of the 30-day follow-up, the fixed effects models were used, without subgroup analysis. Other follow-up results showed that the I^2 value was $> 50\%$. Subgroup analysis was carried out according to different prognostic factors. However, the source of heterogeneity could not be accurately identified, thus the random effects model was used. Sensitivity analysis indicated that the results of each group were relatively stable and reliable.

3.4. MACE

Pooled analysis of 15 studies (n=230,477) shows that the incidence of MACE was lower in male patients with coronary artery disease after PCI compared with females in follow-up period of < 1-year (OR 0.67, 95% CI 0.56–0.80, $P < .001$, $I^2 = 88\%$)^[3,7,11,13,14,17,18,25,26,30,36,37,38,53,56] (Fig. 5). The male patients also experienced lower rate of MACE than females when the follow-up period was extended to at least 1-year [OR 0.84, 95% CI 0.76–0.93, $P < .001$, $I^2 = 74\%$; 17 studies

Table 1
Characteristics of included studies.

Study	Gender	Total patients	Age, years	Hypertension	Diabetes	Dyslipidemia	Smoking	Cardiogenic shock
Cheng et al, 2004	M/W	874/158	61 ± 12/67 ± 11	393/106	199/61	370/65	570/8	102/27
Zimmermann et al, 2009	M/W	405/161	61 ± 13/69 ± 13	254/127	116/60	271/108	267/55	32/14
Bufe et al, 2010	M/W	376/124	58 ± 11/65 ± 12	248/68	42/30	178/62	253/50	38/14
Ferrante et al, 2011	M/W	343/138	53.6~70.8/63.2~80.1	187/94	65/38	166/67	163/42	NS
Ferrante et al, 2012	M/W	565/179	53~72/62~78	308/118	80/28	213/73	226/51	NS
Pu et al, 2011	M/W	446/148	61.3 ± 11.3/70.4 ± 9.3	222/96	80/47	90/22	337/23	NS
Dziewierz et al, 2013	M/W	814/272	51~71/60~79	NS	115/53	NS	319/71	NS
Wijnbergen et al, 2013	M/W	668/202	59.0 ± 10.7/64.7 ± 11.7	167/87	58/30	194/49	439/109	NS
Birkemeyer et al, 2014	M/W	823/281	61 ± 12/69 ± 11	478/191	165/79	379/116	379/65	82/28
Motowska et al, 2008	M/W	371/159	61.7/66.7	127/81	58/40	NS	107/59	NS
Zanchi et al, 2009	M/W	364/124	60.3/67.3	203/93	125/45	173/60	187/34	NS
Otten et al, 2013	M/W	4991/1755	48~77/48~80	1489/740	486/284	1073/341	2331/704	NS
Zhang et al, 2010	M/W	1574/468	63.9 ± 11.3/71.7 ± 8.8	803/322	348/171	624/210	1033/46	NS
Jakobsen et al, 2012	M/W	5405/1980	NS	NS	NS	NS	NS	NS
Meller et al, 2013	M/W	935/366	49~66/57~75	406/219	139/93	341/166	341/132	NS
Mrdovic et al, 2013	M/W	1533/563	NS	NS	NS	NS	NS	NS
Toyota et al, 2013	M/W	3182/1197	64.5 ± 11.7/74.1 ± 10.9	2442/966	1046/380	NS	1652/175	270/128
Pain et al, 2013	M/W	5429/1875	61.1 ± 12.2/67.9 ± 11.9	2350/1012	1096/444	2177/804	1529/370	NS
Velders et al, 2013	M/W	2615/868	61.8 ± 11.9/67.6 ± 13.1	841/394	264/122	608/187	1222/344	NS
Gevaert et al, 2014	M/W	6153/1920	60.7/68.2	2455/1056	868/355	NS	NS	NS
Jackson et al, 2011	M/W	6229/2542	58.3/65.1	4012/1891	1289/689	NS	2921/1037	NS
de Boer et al, 2014	M/W	8588/3343	61.3 ± 11.5/66.2 ± 12.1	3726/1851	1364/690	6680/2533	2496/781	153/62
Benamer et al, 2011	M/W	13,096/3664	59.3/69.7	NS	2016/687	NS	NS	522/246
Al-Fiadh et al, 2011	M/W	2151/802	62.17 ± 12.3/69.6 ± 11.6	1156/564	422/217	NS	1513/388	71/35
Elkoustaf et al, 2006	M/W	816/381	62.6 ± 12.8/68.0 ± 12.3	538/320	251/119	634/304	193/86	NS
Ordoubadi et al, 2012	M/W	1268/372	63.1 ± 11.8/67.8 ± 10.5	782/265	330/132	793/235	822/127	NS
Glaser et al, 2006	M/W	3030/1565	NS	1985/1360	1610/654	2170/1200	2285/943	NS
Hiraka wa et al, 2006	M/W	1033/303	61 ± 18/69 ± 22	345/148	230/91	132/35	686/66	NS
Kumbhani et al, 2012	M/W	1177/697	64.6 ± 11.7/68.0 ± 12.60	NS	443/301	NS	256/114	NS
Liu et al, 2014	M/W	303/162	78.4 ± 3.2/78.7 ± 3.2	228/130	100/67	160/78	62/45	NS
Takagi et al, 2016	M/W	814/212	67.8 ± 9.9/69.9 ± 10.5	615/170	295/102	544/144	NS	NS
Pendyala et al, 2013	M/W	4455/2474	63 ± 12/67 ± 13	3649/2187	1387/1023	3842/2101	2673/1108	221/139
Yang et al, 2017	M/W	3365/1355	61.6 ± 10.9/66.5 ± 9.3	1986/997	679/399	888/381	NS	NS
Wada et al, 2017	M/W	1619/390	64.5 ± 14.6/69.7 ± 8.8	1145/301	NS	NS	1207/116	NS
Numasawa, et al, 2016	M/W	31,915/11,326	68.7 ± 11.4/75 ± 10.3	23,512/8747	12,952/4533	19,657/7030	12,042/1171	825/303
Kunadian et al, 2017	M/W	33,846/2,119,799	63.78/68.49	168,218/97,268	59,391/23,669	182,338/65,535	178310/50,457	5573/2367
Kanic et al, 2017	M/W	2514/1110	62.7/69.3	999/471	295/161	839/332	NS	104/60
Jarrah et al, 2017	M/W	1926/500	57.2 ± 4.9/62.9 ± 5.5	1104/407	840/328	893/291	992/63	NS
Idris et al, 2017	M/W	2265/747	43~75/41~80	1173/485	529/231	1547/515	727/148	73/29
Heer et al, 2017	M/W	125,918/48,717	53~75/61~81	NS	28,782/13,880	NS	NS	NS
Farmer et al, 2017	M/W	63,717/1040	60.1~70.6/54.7~65.8	57,807/913	31,246/495	57,575/898	NS	NS
Chandrasekha r, et al, 2016	M/W	3689/1162	48.6 ± 5.6/48.1 ± 6.0	2580/859	1029/476	2802/898	1674/571	NS
Ng et al, 2015	M/W	11,004/3780	61.1 ± 11.0/65.6 ± 11.5	6624/2721	2520/1134	NS	3752/1077	NS
Lempereur et al, 2014	M/W	95,030/35,955	64.8 ± 11.6/70.3 ± 11.3	50,270/22,759	19,291/9635	55,498/21,177	64,240/12,656	1806/755
Kanic et al, 2016	M/W	1472/597	61.8 ± 12.0/68.3 ± 12.6	547/234	146/82	472/179	NS	92/50
Numasawa et al, 2015	M/W	8114/2106	66.6 ± 10.8/72.7 ± 9.7	5924/1629	3421/865	5309/1435	3257/300	NS
Perl et al, 2015	M/W	1075/271	60 ± 13/69 ± 13	415/171	215/73	490/151	580/92	NS
Imami et al, 2015	M/W	611/221	61.8 ± 12.3/71.2 ± 12.1	223/111	128/46	126/54	259/71	NS
Barthélemy et al, 2015	M/W	593/182	69 ± 15/70 ± 15	251/102	108/33	233/63	NS	NS

M/W = Man/Woman, NS = Not Statement.

Table 2
The ischemia-reperfusion time between different genders were mentioned in this study.

Study	Gender	Symptom onset time, minutes	Door-to-balloon time, minutes	Reperfusion time, minutes
Cheng et al, 2004	M/W	186 ± 155/205 ± 148	NS	284 ± 172/317 ± 175
Zimmermann et al, 2009	M/W	236 ± 263/262 ± 235	63 ± 58/57 ± 45	NS
Bufe et al, 2010	M/W	NS	NS	230 ± 157/254 ± 168
Ferrante et al, 2011	M/W	140~395/165-485	52~117/57~148	NS
Ferrante et al, 2012	M/W	145~315/150-320	70~138/74~164	NS
Pu et al, 2011	M/W	NS	NS	246 ± 174/294 ± 174
Dziewierz et al, 2013	M/W	NS	NS	140~340/145-359
Wijnbergen et al, 2013	M/W	176 ± 119/204 ± 135	16 ± 7/16 ± 6	193 ± 119/220 ± 135
Otten et al, 2013	M/W	NS	70~73/30~73	NS
Zhang et al, 2010	M/W	NS	NS	351 ± 176/362 ± 168
Meller et al, 2013	M/W	NS	NS	229.8/295.8
Velders et al, 2013	M/W	128~279/141~286	33~67/33~68	NS
Perl et al, 2015	M/W	596 ± 367/815 ± 460	44 ± 40/45 ± 17	NS

M/W = man/woman, NS = not statement.

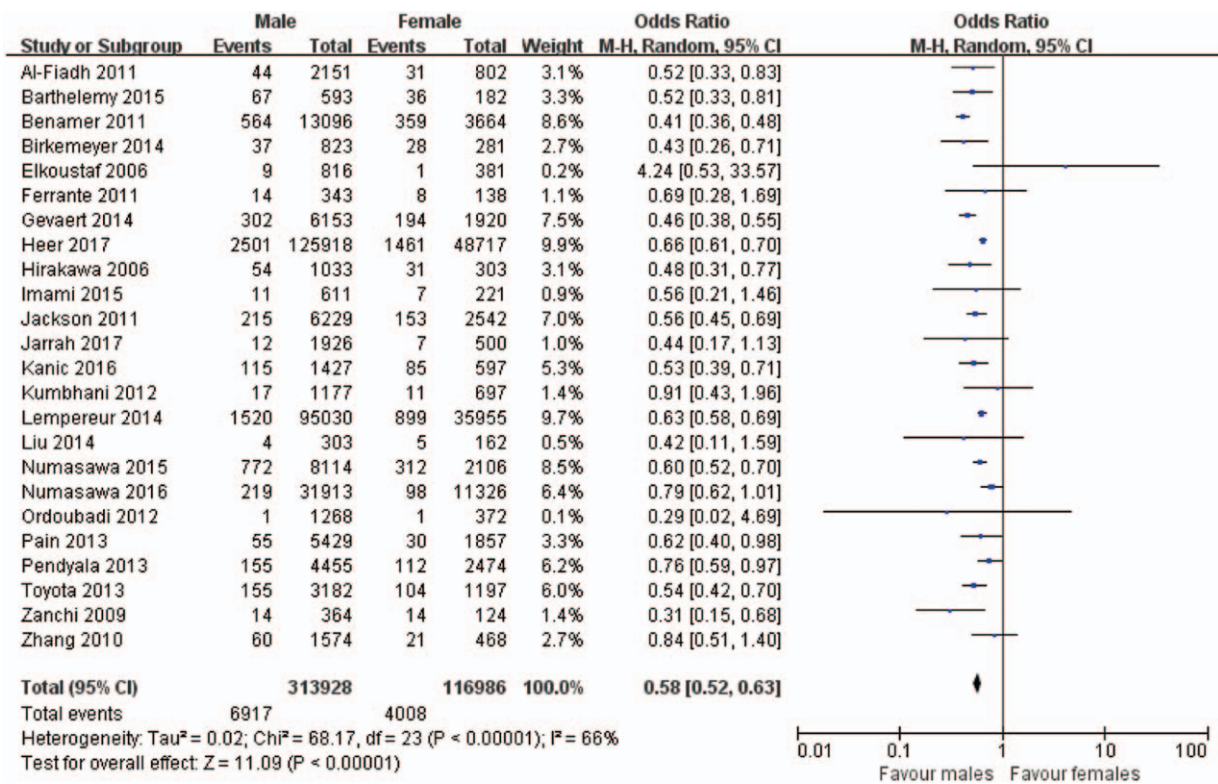


Figure 1. Forest plot of in-hospital mortality in male vs female patients with coronary artery disease after PCI. PCI =percutaneous coronary intervention.

(n = 111,903)^[4–6,13,17,18,25,26,29,30,31,36,38,52,54–56] (Fig. 6). The results of both groups displayed that the I^2 value was >50%, but the appropriate factors for the high heterogeneity after adopted the subgroup analysis cannot be identified. Therefore, the meta-

analysis of MACE was performed by random effects model. Sensitivity analysis showed that no single study was responsible for the overall effect size, and the results were stable and credible.

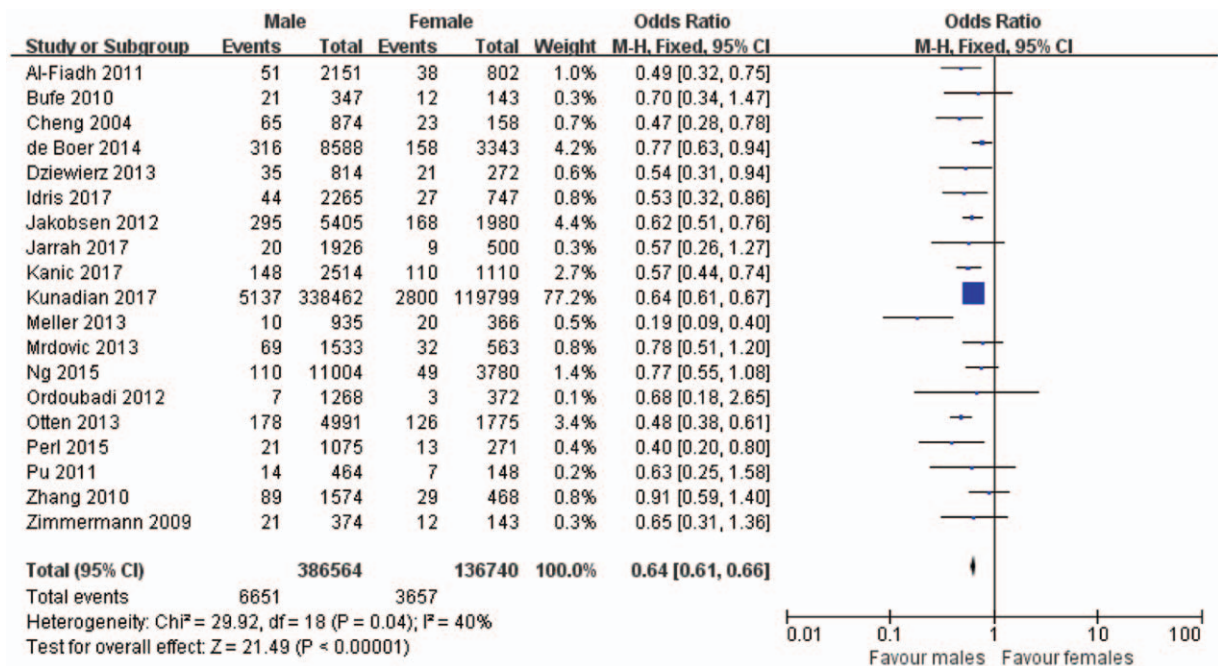


Figure 2. Forest plot of 30-day mortality in male vs female patients with coronary artery disease after PCI. PCI =percutaneous coronary intervention.

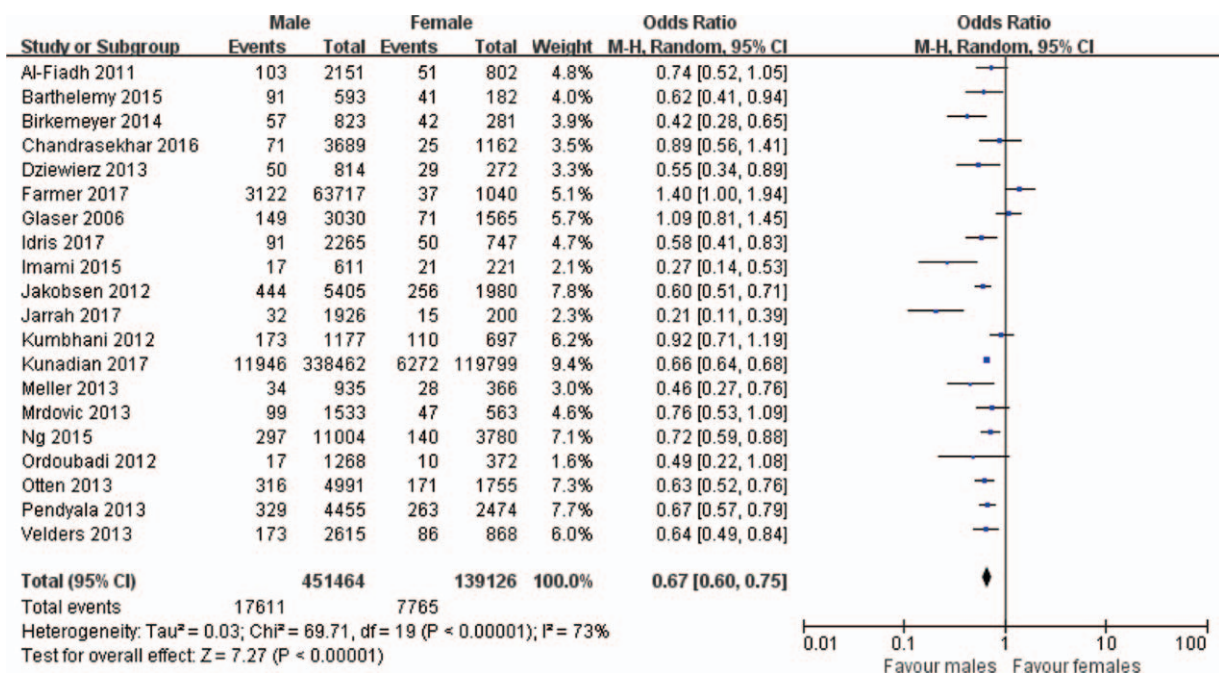


Figure 3. Forest plot of 1-year mortality in male vs female patients with coronary artery disease after PCI. PCI =percutaneous coronary intervention.

3.5. The revascularization

The pooled data show that the revascularization rate in male patients with coronary artery disease after PCI was lower than that of females during a follow-up period of <1-year [OR 0.93, 95% CI 0.69–1.26, P<.001, I²=64%; 9 studies (n = 39,375)]^[2,13,14,25,26,35,36,53,56] (Fig. 7), which was on opposite to the outcomes between male and female patients for at least 1-year [OR 1.17, 95% CI 1.00–1.36, P < .001, I² = 71%; 16 studies (n = 37,770)]^[4–6,9,10,13,18,25,26,29,30,35,36,44,52,56] (Fig. 8). The result showed that the I² values of both groups were >50%. Random effects model was utilized, because the heterogeneity cannot be explained according to subgroup analysis. Sensitivity analysis indicated that the result was stable and relatively robust.

4. Discussion

The main results of this meta-analysis are as follows: the mortality in male patients with coronary artery disease after PCI was lower than that of females; the male patients with coronary artery disease after PCI harbored a lower incidence of MACE, no matter whether the follow-up period was <1 year or at least 1 year; the male patients with coronary artery disease after PCI overwhelmed females in long-term revascularization.

The mortality in male patients with coronary artery disease after PCI was lower than that of females in this study both in short-term and long-term follow-up, which was consistent with previous systematic reviews.^[45–48] Because female subjects had much more hypertension, diabetes, dyslipidemia this meta-

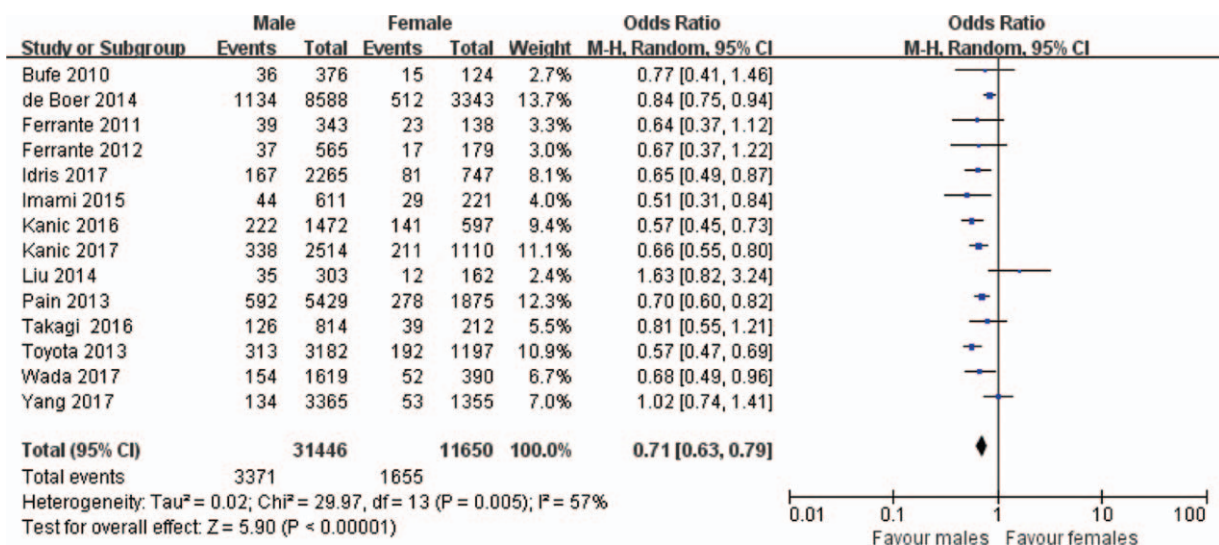


Figure 4. Forest plot of at least 2-years mortality in male vs female patients with coronary artery disease after PCI. PCI =percutaneous coronary intervention.

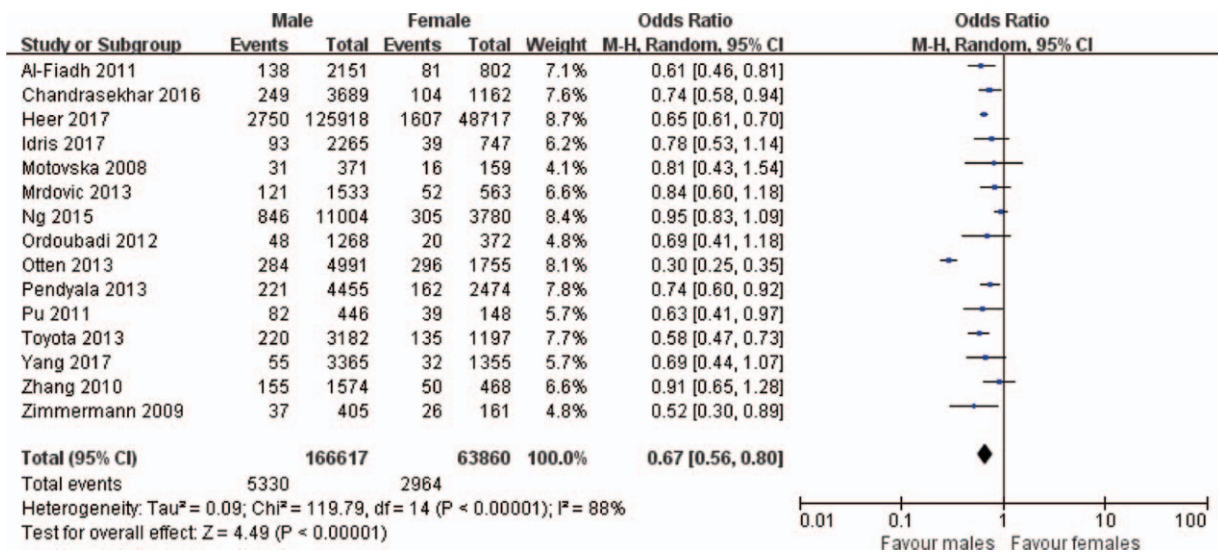


Figure 5. Forest plot of <1-year MACE in male vs female patients with coronary artery disease after PCI. PCI =percutaneous coronary intervention.

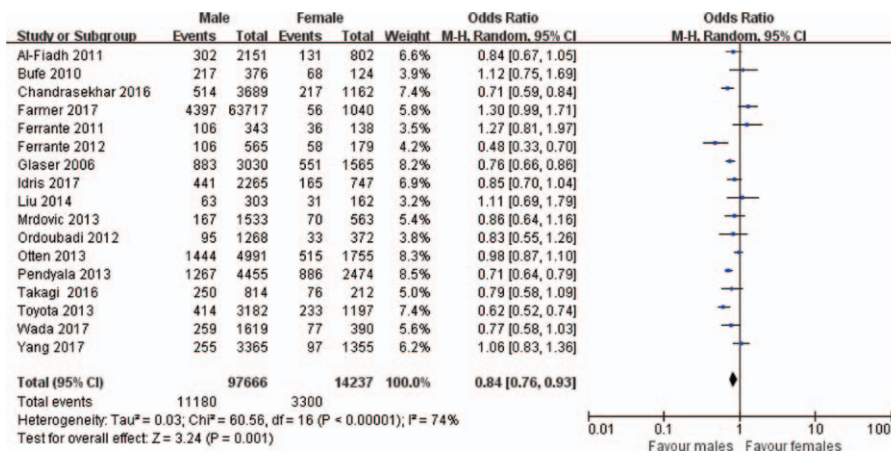


Figure 6. Forest plot of the least 1-year MACE in male vs female patients with coronary artery disease after PCI. PCI =percutaneous coronary intervention.

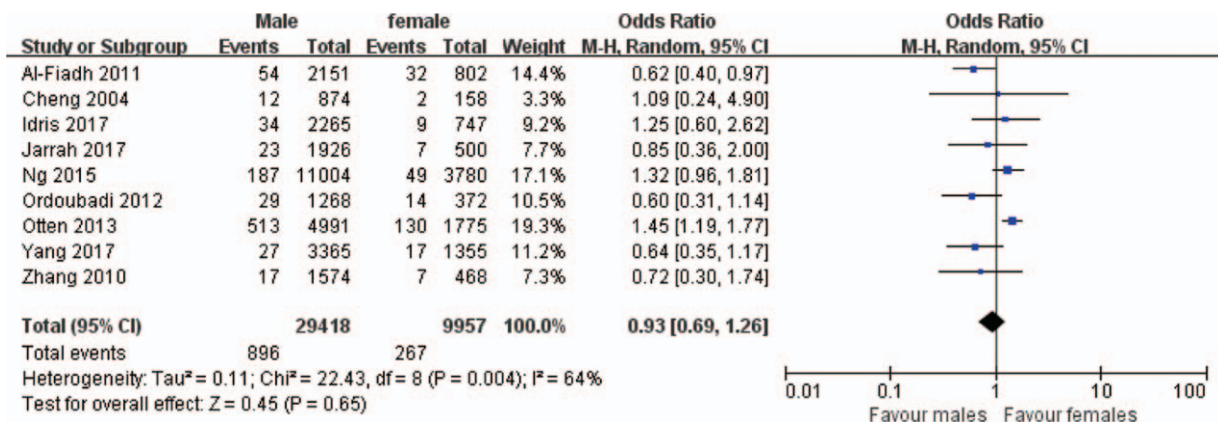


Figure 7. Forest plot of <1-year revascularization rate in male vs female patients with coronary artery disease after PCI. PCI =percutaneous coronary intervention.

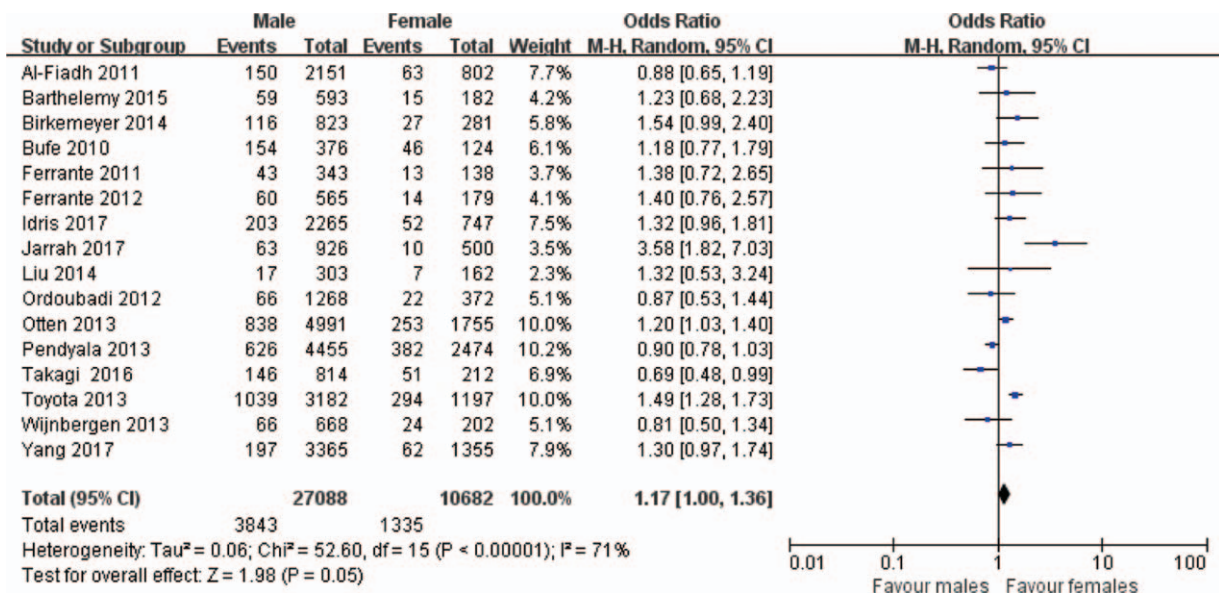


Figure 8. Forest plot of the least 1-year revascularization rate in male vs female patients with coronary artery disease after PCI. PCI =percutaneous coronary intervention.

analysis, especially longer times of reperfusion ischemia,^[1-8,12,13,15,19,41] the latter may be caused by chest pain symptoms, which had not been fully explained in female patients with coronary artery disease, leading to delay prehospital visits. Therefore, the high mortality in female patients with coronary artery disease after PCI had been largely attributed to more adverse cardiovascular risk profiles compared with males. This meta-analysis has confirmed that the female patients with coronary artery disease were older than males, which may also attribute to the high mortality of female patients, and consistent with National Cardiovascular Data Registry ACTION Registry of America.^[57] Meanwhile, in this study, it had also been verified that the female subjects were more prone to suffer from cardiogenic shock, which was considered as another important indicator for higher mortality in female patients with coronary artery disease after PCI. The same consequences were obtained by meta-analysis by Kano et al.^[47] In short, it is an indisputable fact that the mortality in female patients with coronary artery disease after PCI was high.

Similar to the above results, the male patients with coronary artery disease after PCI also had a lower incidence of MACE for <1 year or at least 1-year in this meta-analysis, which is a supplement and summary to previous systematic reviews and observational studies.^[7,25,29,38,54,56] The reasons for the above differences should first be attributed to the fact that the mortality in female patients with coronary artery disease after PCI is higher than that of males. Moreover, possessing more adverse cardiovascular risk profile was also an important factor for high incidence of MACE in female patients with coronary artery disease, the baseline data of this study had witnessed this proposition. The study of Jakobsen et al^[15] also showed female patients with coronary artery disease were burdened with more complications and worse hemodynamic status compared with males. The gender difference of MACE was still largely attributed to the higher incidence of heart failure in female patients with STEMI in some cohort.^[3,6,13,20] In summary, the above pathological factors had led to the high incidence of MACE in

female patients with coronary artery disease after PCI. It is noteworthy that females had a worse clinical outcome, which reminds physicians should pay more attention to female patients in clinical practice.

This systematic review and meta-analysis also showed that male patients with coronary artery disease after PCI had the advantages of revascularization compared with females in the long-term follow-up, which was consistent with the parts of previous observational studies,^[4-6,10,13,18,35,36,44,52,56] and supplied the main outcome of previous systematic reviews.^[45-48] This may be associated with more smoking in males from the baseline data of this study. On the contrary, the low incidence of revascularization in female subjects also included lower follow-up rates, atypical symptoms, difficult identification of myocardial ischemia, unwillingness of receiving invasive examinations, as well as the prejudices of doctor that female subjects might harbor lower rate of coronary arteriography during follow-up.^[17] In addition, female subjects with coronary artery disease after PCI had higher mortality during short and long-term follow-up, which might reduce the chance of next revascularization. Moreover, a research had indicated that the application of drug-eluting stents could decrease probability of coronary artery revascularization in female patients with PCI.^[58] Furthermore, the coronary artery of male patient with coronary artery disease is prone to harbor complicated lesions, including left main disease, chronic total occlusion and diffuse lesion.^[56] Meanwhile, male subjects suffering from more platelet-rich thrombus, atherosclerotic plaque rupture as well as micro-embolization were also demonstrated in some studies.^[59] The above-described pathophysiological difference would result in elevated risks of revascularization in male subjects. However, the female had a high incidence of <1-year revascularization, which was an integral part to <1-year MACE. Overall, the incidence of revascularization in female patients with coronary artery disease after PCI was higher than that of males in short-term follow-up, which was opposite in long-term follow-up showed the opposite result.

4.1. Limitations

Firstly, the main limitations of this study were that all articles included in this study were nonrandomized control studies. Therefore, many subjective factors were inevitable during the follow-up. Secondly, of the 1,032,828 patients included in the meta-analysis, the female patients accounted for only 1/4 of the total sample size. Thus, unequal distribution of gender may lead to a bias. Thirdly, there are large discrepancy in sample size and follow-up spans among different studies, which may lead to heterogeneity. Because most studies had larger heterogeneity, the random effects model was adopted; the results may weaken the large sample information with better quality. Fourthly, due to the lack of patient-level data, subgroup analysis was not conducted according to the type of subjects, and the specific prognosis of patients with different types of coronary artery disease undergoing PCI could not be assessed. Final, the language included in the study was limited to English, and there was a lack of researches in South America and Africa countries. Therefore, language and regional bias may be unavoidable.

5. Conclusions

In conclusion, the prognosis of male patients with coronary artery disease after PCI is better than that of females, except for long-term revascularization.

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References

- [1] World Health Organization. The top 10 causes of death, Fact Sheet No.310. Updated January 2017. Accessed date: Jan 16 2018. Available at: www.who.int/mediacentre/factsheets/fs310/en/.
- [2] Cheng CI, Yeh KH, Chang HW, et al. Comparison of baseline characteristics, clinical features, angiographic results, and early outcomes in male vs female with acute myocardial infarction undergoing primary coronary intervention. *Chest* 2004;126:47–53.
- [3] Zimmermann S, Ruthrof S, Nowak K, et al. Short-term prognosis of contemporary interventional therapy of ST-elevation myocardial infarction: does gender matter? *Clin Res Cardiol* 2009;98:709–15.
- [4] Bufe A, Wolfertz J, Dinh W, et al. Gender-based differences in long-term outcome after ST-elevation myocardial infarction in patients treated with percutaneous coronary intervention. *J Females Health* 2010;19:471–5.
- [5] Ferrante G, Corrada E, Belli G, et al. Impact of female sex on long-term outcomes in patients with ST-elevation myocardial infarction treated by primary percutaneous coronary intervention. *Can J Cardiol* 2011;27:749–55.
- [6] Ferrante G, Presbitero P, Corrada E, et al. Sex-specific benefits of sirolimus-eluting stent on long-term outcomes in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention: insights from the Multicenter Evaluation of Single High-Dose Bolus Tirofiban versus abciximab with sirolimus-eluting stent or bare-metal stent in acute myocardial infarction study trial. *Am Heart J* 2012;163:104–11.
- [7] Pu J, Shan P, Ding S, et al. Gender differences in epicardial and tissue-level reperfusion in patients undergoing primary angioplasty for acute myocardial infarction. *Atherosclerosis* 2011;215:203–8.
- [8] Dziewierz A, Siudak Z, Rakowski T, et al. Early administration of abciximab reduces mortality in female patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention (from the EUROTRANSFER Registry). *J Thromb Thrombolysis* 2013;36:240–6.
- [9] Wijnbergen I, Tijssen J, van't Veer M, et al. Gender differences in long-term outcome after primary percutaneous intervention for ST-segment elevation myocardial infarction. *Catheter Cardiovasc Interv* 2013;82:379–84.
- [10] Birkemeyer R, Schneider H, Rillig A, et al. Do gender differences in primary PCI mortality represent a different adherence to guideline recommended therapy? a multicenter observation. *BMC Cardiovasc Disord* 2014;14:71.
- [11] Motovska Z, Widimsky P, Aschermann M. The impact of gender on outcomes of patients with ST elevation myocardial infarction transported for percutaneous coronary intervention: analysis of the PRAGUE-1 and 2 studies. *Heart* 2008;94:e5.
- [12] Zanchi J, Miric D, Giunio L, et al. Gender differences in in-hospital mortality and angiographic findings of patients with acute ST-segment elevation myocardial infarction (STEMI) undergoing percutaneous coronary intervention (PCI). *Coll Antropol* 2009;33:1359–62.
- [13] Otten AM, Maas AH, Ottervanger JP, et al. Is the difference in outcome between male and female treated by primary percutaneous coronary intervention age dependent? Gender difference in STEMI stratified on age. *Eur Heart J Acute Cardiovasc Care* 2013;2:334–41.
- [14] Zhang Q, Qiu JP, Zhang RY, et al. Absence of gender disparity in short-term clinical outcomes in patients with acute ST-segment elevation myocardial infarction undergoing irolimus-eluting stent based primary coronary intervention: a report from Shanghai Acute Coronary Event (SACE) Registry. *Chin Med J* 2010;123:782–8.
- [15] Jakobsen L, Niemann T, Thorsgaard N, et al. Sex- and age-related differences in clinical outcome after primary percutaneous coronary intervention. *Eurointervention* 2012;8:904–11.
- [16] Meller SM, Lansky AJ, Costa RA, et al. Implications of myocardial reperfusion on survival in female versus male with acute myocardial infarction undergoing primary coronary intervention. *Am J Cardiol* 2013;112:1087–92.
- [17] Mrdovic I, Savic L, Asanin M, et al. Sex-related analysis of short- and long-term clinical outcomes and bleeding among patients treated with primary percutaneous coronary intervention: an evaluation of the RISK-PCI data. *Can J Cardiol* 2013;29:1097–103.
- [18] Toyota T, Furukawa Y, Ehara N, et al. Sex-based differences in clinical practice and outcomes for Japanese patients with acute myocardial infarction undergoing primary percutaneous coronary intervention. *Circ J* 2013;77:1508–17.
- [19] Pain TE, Jones DA, Rathod KS, et al. Influence of female sex on long-term mortality after acute coronary syndromes treated by percutaneous coronary intervention: a cohort study of 7304 patients. *Coron Artery Dis* 2013;24:183–90.
- [20] Velders MA, Boden H, van Boven AJ, et al. Influence of gender on ischemic times and outcomes after ST-elevation myocardial infarction. *Am J Cardiol* 2013;111:312–8.
- [21] Gevaert SA, De BD, Evrard P, et al. Gender, TIMI risk score and in-hospital mortality in STEMI patients undergoing primary PCI: results from the Belgian STEMI registry. *Eurointervention* 2014;9:1095–101.
- [22] Jackson EA, Moscucci M, Smith DE, et al. The association of sex with outcomes among patients undergoing primary percutaneous coronary intervention for ST elevation myocardial infarction in the contemporary era: Insights from the Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BMC2). *Am Heart J* 2011;161:106–12.
- [23] de Boer SP, Roos-Hesslink JW, van Leeuwen MA, et al. Excess mortality in female compared to male after PCI in STEMI: an analysis of 11, 931 patients during 2000–2009. *Int J Cardiol* 2014;176:456–63.
- [24] Benamer H, Tafflet M, Bataille S, et al. Female gender is an independent predictor of in-hospital mortality after STEMI in the era of primary PCI: insights from the greater Paris area PCI Registry. *Eurointervention* 2011;6:1073–9.

- [25] Al-Fiadh AH, Andrianopoulos N, Farouque O, et al. Contemporary outcomes in female undergoing percutaneous coronary intervention for acute coronary syndromes. *Int J Cardiol* 2011;151:195–9.
- [26] Fath-Ordoubadi F, Barac Y, Abergel E, et al. Gender impact on prognosis of acute coronary syndrome patients treated with drug-eluting stents. *Am J Cardiol* 2012;110:636–42.
- [27] Hirakawa Y, Masuda Y, Uemura K, et al. Differences in in-hospital mortality between male and female with acute myocardial infarction undergoing percutaneous coronary intervention in Japan: Tokai Acute Myocardial Infarction Study (TAMIS). *Am Heart J* 2006;151:1271–5.
- [28] Kumbhani DJ, Shishehbor MH, Karim S, et al. Influence of gender on long-term mortality in patients presenting with non-ST-elevation acute coronary syndromes undergoing percutaneous coronary intervention. *Am J Cardiol* 2012;109:1087–91.
- [29] Takagi K, Chieffo A, Shannon J, et al. Impact of gender on long-term mortality in patients with unprotected left main disease: The Milan and New-Tokyo (MITO) Registry. *Int J Cardiol* 2014;177:1131–3.
- [30] Pendyala LK, Torguson R, Loh JP, et al. Comparison of adverse outcomes after contemporary percutaneous coronary intervention in female versus male with acute coronary syndrome. *Am J Cardiol* 2013;111:1092–8.
- [31] Wada H, Ogita M, Miyauchi K, et al. Impact of gender difference on long-term outcomes of percutaneous coronary intervention for coronary artery disease in patients under statin treatment. *Heart Vessels* 2017;32:16–21.
- [32] Numasawa Y, Inohara T, Ishii H, et al. Comparison of outcomes of female versus male with non-ST-elevation acute coronary syndromes undergoing percutaneous coronary intervention (from the Japanese Nationwide Registry). *Am J Cardiol* 2017;119:826–31.
- [33] Kunadian V, Qiu W, Lagerqvist B, et al. Gender differences in outcomes and predictors of all-cause mortality after percutaneous coronary intervention (data from United Kingdom and Sweden). *Am J Cardiol* 2017;119:210–6.
- [34] Kanic V, Vollrath M, Tapajner A, et al. Sex-Related 30-Day and long-term mortality in acute myocardial infarction patients treated with percutaneous coronary intervention. *J Females Health* 2017;26:374–9.
- [35] Jarrah MI, Hammoudeh AJ, Alnatour DB, et al. Gender differences in risk profile and outcome of Middle Eastern patients undergoing percutaneous coronary intervention. *Saudi Med J* 2017;38:149–55.
- [36] Idris H, French JK, Shugman IM, et al. Influence of age and gender on clinical outcomes following percutaneous coronary intervention for acute coronary syndromes. *Heart Lung Circ* 2017;26:554–65.
- [37] Heer T, Hochadel M, Schmidt K, et al. Sex differences in percutaneous coronary intervention—insights from the coronary angiography and PCI registry of the German society of cardiology. *J Am Heart Assoc* 2017;6:e004972.
- [38] Chandrasekhar J, Usman Baber MD, Sartori S, et al. Sex-related differences in outcomes among male and female under 55 years of age with acute coronary syndrome undergoing percutaneous coronary intervention: Results from the PROMETHEUS Study. *Catheter Cardiovasc Interv* 2016;89:629–37.
- [39] Lempereur M, Magne J, Cornelis K, et al. Impact of gender difference in hospital outcomes following percutaneous coronary intervention. Results of the Belgian Working Group on Interventional Cardiology (BWGIC) registry. *Eurointervention* 2014;12:e216–223.
- [40] Kanic V, Vollrath M, Naji FH, et al. Gender related survival differences in ST-elevation myocardial infarction patients treated with primary PCI. *Int J Med Sci* 2016;13:440–4.
- [41] Numasawa Y, Kohsaka S, Miyata H, et al. Gender differences in in-hospital clinical outcomes after percutaneous coronary interventions: an insight from a Japanese multicenter registry. *PLoS One* 2015;10:e0116496.
- [42] Michal Laufer-Perl MD, Yacov Shacham MD, Sivan Letourneau-Shesaf MD, et al. Gender-related mortality and in-hospital complications following ST-segment elevation myocardial infarction: data from a primary percutaneous coronary intervention cohort. *Clin Cardiol* 2015;38:145–9.
- [43] Ghauharali-Imami S, Bax M, Haasdijk A, et al. The impact of gender on long-term mortality in patients with multivessel disease after primary percutaneous coronary intervention. *Netherlands Heart J* 2015;23:592–9.
- [44] Barthélémy O, Degrell P, Berman E, et al. Sex-related differences after contemporary primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. *Arch Cardiovasc Dis* 2015;108:428–36.
- [45] Bavishi C, Bangalore S, Patel D, et al. Short and long-term mortality in female and male undergoing primary angioplasty: a comprehensive meta-analysis. *Int J Cardiol* 2015;198:123–30.
- [46] Mg VDM, Nathoe HM, Van d GY, et al. Worse outcome in female with STEMl: a systematic review of prognostic studies. *Eur J Clin Invest* 2015;45:226–35.
- [47] Conrotto F, D’Ascenzo F, Humphries KH, et al. A meta-analysis of sex-related differences in outcomes after primary percutaneous intervention for ST-segment elevation myocardial infarction. *J Interv Cardiol* 2015;28:132–40.
- [48] Jang JS, Park YA, Jin HY, et al. P4661Sex difference in mortality among patients with acute myocardial infarction treated by primary percutaneous coronary intervention: a meta-analysis. *Eur Heart J* 2017;38(suppl 1):
- [49] Higgins JPT, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration’s tool for assessing risk of bias in randomized trials. *Brit Med J* 2011;343:d5928.
- [50] Stang A. Critical evaluation of the Newcastle–Ottawa scale for the assessment of the quality of non-randomized studies in meta-analyses. *Eur J Epidemiol* 2010;25:603–5.
- [51] Elkoustaft RA, Mamkin I, Mather JF, et al. Comparison of results of percutaneous coronary intervention for non-ST-elevation acute myocardial infarction or unstable angina pectoris in male versus female. *Am J Cardiol* 2006;98:182–6.
- [52] Liu Y, Hu X, Xue Q, et al. Influence of sex on outcomes after percutaneous coronary intervention in patients over 75 years of age with coronary heart disease. *Clin Interv Aging* 2014;9:1831–7.
- [53] Ng VG, Baumbach A, Grinfeld L, et al. Impact of bleeding and bivalirudin therapy on mortality risk in female undergoing percutaneous coronary intervention (from the REPLACE-2, ACUITY, and HORIZONS-AMI Trials). *Am J Cardiol* 2015;117:186–91.
- [54] Farmer MM, Stanislawski MA, Plomondon ME, et al. Sex differences in 1-year outcomes after percutaneous coronary intervention in the Veterans Health Administration. *J Females Health* 2017;26:1062–8.
- [55] Glaser R, Selzer F, Jacobs AK, et al. Effect of gender on prognosis following percutaneous coronary intervention for stable angina pectoris and acute coronary syndromes. *Am J Cardiol* 2006;98:1446–50.
- [56] Yang J, Zhang F, Qian J, et al. Sex-based influence on clinical outcomes after drug-eluting stent implantation in real-world patients: insight from the FOCUS registry. *Ann Med* 2017;49:185–95.
- [57] Smilowitz NR, Mahajan AM, Roe MT, et al. Mortality of myocardial infarction by sex, age, and obstructive coronary artery disease status in the ACTION Registry-GWTG (Acute Coronary Treatment and Intervention Outcomes Network Registry-Get With the Guidelines). *Circ Cardiovasc Qual Outcomes* 2017;10:e003443.
- [58] Iyanoye A, Moreyra AE, Swerdel JN, et al. Gender disparity in the use of drug-eluting stents during percutaneous coronary intervention for acute myocardial infarction. *Catheter Cardiovasc Interv* 2015;86:221–8.
- [59] Wiviott SD, Cannon CP, Morrow DA, et al. Differential expression of cardiac biomarkers by gender in patients with unstable angina/non-ST-elevation myocardial infarction: a TACTICS-TIMI 18 (Treat Angina with Aggrastat and determine Cost of Therapy with an Invasive or Conservative Strategy-Thrombolysis In Myocardial Infarction 18) substudy. *Circulation* 2004;109:580–6.