

Original Research

The Late-Term Pregnancy Proportion of Women Experiencing Postpartum Hemorrhage and Symptomatic Fibroids Following Uterine Artery Embolization: A Meta-Analysis

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Abstract

Background: There are short of systematical analyze of the late-term pregnancy proportion of women experiencing postpartum hemorrhage and symptomatic fibroids following uterine artery embolization (UAE). **Methods:** This was a systematic literature review and meta-analysis of existing studies. **Results:** In total, we identified 497 pregnancies following UAE; 49 patients chose to abort their pregnancies, 79 miscarried during the early- or middle-terms of pregnancy, and 378 pregnancies successfully progressed into the late-term (>28 weeks). When considering the included studies, 58.33%–100% of pregnancies successfully reached the late-term. When considering all studies, the proportion of subjects achieving a late-term pregnancy was 96% (95% confidence interval [CI], 90%–100%) when using a random model ($I^2 = 21.08$, $p < 0.001$). With regards to the methods used to perform embolization, the proportion of late-term pregnancies were 92% (95% CI, 79%–100%) in the absorbable Embosphere group and 88% (95% CI, 79%–95%) in the non-absorbable Embosphere group. The proportion of patients achieving late-term pregnancy after UAE was 93% (95% CI, 85%–93%) in the group experiencing postpartum hemorrhage and 82% (95% CI, 73%–90%) in those with symptomatic fibroids. **Conclusions:** Our analyses indicate that patients have a good chance of a successful pregnancy if they experience postpartum hemorrhage patients and symptomatic fibroids patients if they wish to preserve their fertility.

Keywords: late-term pregnancy proportion; postpartum hemorrhage; symptomatic fibroids; uterine artery embolization; meta-analysis

1. Introduction

Uterine artery embolization (UAE) was is a commonly applied approach to preserve organs and treat obstetric hemorrhage, symptomatic uterine fibroids, and uterine adenomyosis [1]. A significant body of evidence now supports the fact that UAE is a safe and effective alternative to hysterectomy for the alleviation of obstetric or gynecological bleeding, or to relieve the pain associated with uterine adenomyosis [2]. An increasing number of reports have described successful pregnancy following UAE, thus demonstrating that women can achieve successfully achieve pregnancy and deliver healthy offspring [3]. However, because UAE can influence the supply of blood to the uterus, this technique also increases the risks of adverse pregnancy outcomes, especially with regards to late-term pregnancies (>28 weeks). Indeed, the American College of Obstetricians and Gynecologists recommended that UAE should applied cautiously in women who wish to retain their fertility [4]. At present, UAE is mostly applied on women of advanced age. In a previous study, Hayden reported an increase in miscarriage, but not critical adverse obstetric sequelae arising from intrauterine growth retardation (IUGR) and prematurity following the use of UAE to treat symptomatic fibroids [5]. However, previous studies did not determine the proportion of women experiencing and wish-

ing to keep late-term pregnancies following UAE treatment. In the present study, we wanted to identify evidence in the existing literature that could be drawn upon to counsel patients with regards to late-term pregnancy after UAE. To investigate late-term pregnancy outcomes after UAE, we conducted an intensive review of the existing literature, focusing on articles that had been published in English. The aim of this study was two points to be clear: first, to provide an exactly outcomes of UAE pregnancies; and second, to compare pooled data from UAE pregnancies with regards to non-absorbable Embospheres and absorbable Embospheres, symptomatic multiple fibroids, and postpartum hemorrhage. Our study design aimed to investigate how embolization, or its sequelae, might influence late-term pregnancies.

2. Materials and Methods

2.1 Search Strategy

Relevant studies were identified by searching the MEDLINE, EMBASE, Cochrane, OVID, and PubMed, databases using the search terms “uterine artery embolization”, “uterine artery obstruction”, “UAE”, and “pregnancy”. The reference lists of the retrieved articles were then hand-searched to identify additional studies. Studies were included if they described complete pregnancies af-



ter a series of UAE cases. We excluded cases involving ectopic pregnancies and voluntary terminations following UAE. Individual case reports were excluded. Our analyses were based on late-term pregnancy (in which delivery occurred after >28 weeks of gestation).

2.2 Statistical Analysis

Statistical analysis was performed using the Stata 15 meta-analysis package. Summary statistics for age are presented as means \pm SD; for categorical variables, we used odds ratios (ORs) and 95% confidence intervals (CIs). Comparisons between categorical data were analyzed using tables in combination with Fisher's exact test. p values less than 0.05 (two-tailed) were considered to be statistically significant.

3. Results

3.1 Summary of the Studies Included in this Meta-Analysis

A detailed flowchart of the selection process is shown in Fig. 1. In total, 29 studies met the inclusion criteria and were included in our study; these are summarized in Table 1 (Ref. [6–34]). Analysis of the selected publications revealed that long-term follow-up data after UAE were available for 497 women. The 29 studies included in our meta-analysis reported 3 to 56 pregnancies per study when considered at the longest reported follow-up point. Analysis showed that 49 cases selected abortion to terminate their pregnancy, while 79 experienced miscarriage during early- or middle-term pregnancy; 378 pregnancies lasted to the late-term (>28 weeks). After excluding voluntary terminations, the successful proportion of late term pregnancy was 58.33% to 100%.

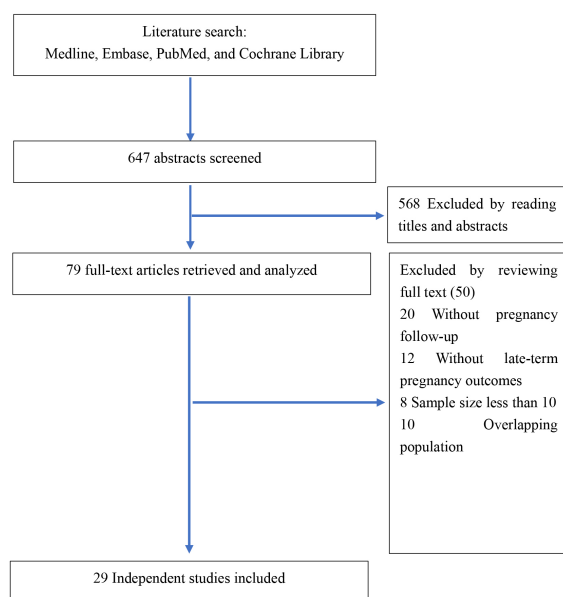


Fig. 1. Flowchart shows selection of studies.

3.2 Levels of Heterogeneity after the Included Studies were Pooled

After excluding cases involving ectopic pregnancies or voluntary termination, the collective proportion of miscarriage was 17.63% (79/448); the lowest rate was 0% and the highest rate was 30.35% (17/56). The pooled late rate among 448 pregnancies 84.59%, among the 29 studies. After we pooled all of the studies, the proportion of women achieving late-term pregnancy was 96% (95% CI, 90%–100%) in a random model ($I^2 = 21.08$, $p < 0.001$); it was also evident that there was significant heterogeneity (Fig. 2). Collectively, our data showed that a high proportion of late-term pregnancies had been achieved in patients who had experienced postpartum hemorrhage and symptomatic fibroids after UAE.

3.3 The Effects of Embolic Agents in Pregnancy Women after UAE

Of the 29 studies selected for analysis, 19 studies provided information relating to the embolic agents that were used. Absorbable embolic agents were used in 6 studies [6,11,17,25,26,29] including 94 pregnancies; of these pregnancies, there were 13 early miscarriages, 5 ectopic pregnancies or voluntary terminations, and 76 pregnancies continued to late-term. When pooled, after excluding ectopic pregnancies or voluntary terminations, we found that late term pregnancy rate was 92% (95% CI, 79%–100%, $I^2 = 10.58$, $p = 0.06$) in a random model. There was no significant heterogeneity between these studies (Fig. 3A).

Non-absorbable embolic agents were used in 13 studies [7–9,13,14,16,19–21,24,27,28,32] and involved the treatment of 206 pregnancies. Of these, there were 28 cases of early miscarriage, 30 ectopic pregnancies or voluntary termination cases; 149 pregnancies lasted to the late-term. The late-term pregnancy rate was 88% (95% CI, 79%–95%, $I^2 = 20.29$, $p = 0.06$) in a random model. There was no significant heterogeneity between these studies (Fig. 3B).

3.4 Late-Term Pregnancies in Females Undergoing UAE Treatment as a Result of Obstetric Hemorrhage and Symptomatic Fibroids

Of the selected studies, 14 reported the use of UAE to treat postpartum hemorrhage [6,9–11,16,18,22,23,25,26,29,31,34]; collectively, these studies reported 205 pregnancies, 24 miscarriages, and 16 voluntary terminations; 165 pregnancies continued to the late-term. Next, we pooled data relating to pregnancies in females who underwent UAE because of postpartum hemorrhage. The late-term pregnancy rate was 93% (95% CI, 85%–93%, $I^2 = 24.81$, $p = 0.02$) in a random model. We identified significant heterogeneity ($p = 0.02$) between these studies (47.61%) (Fig. 4A).

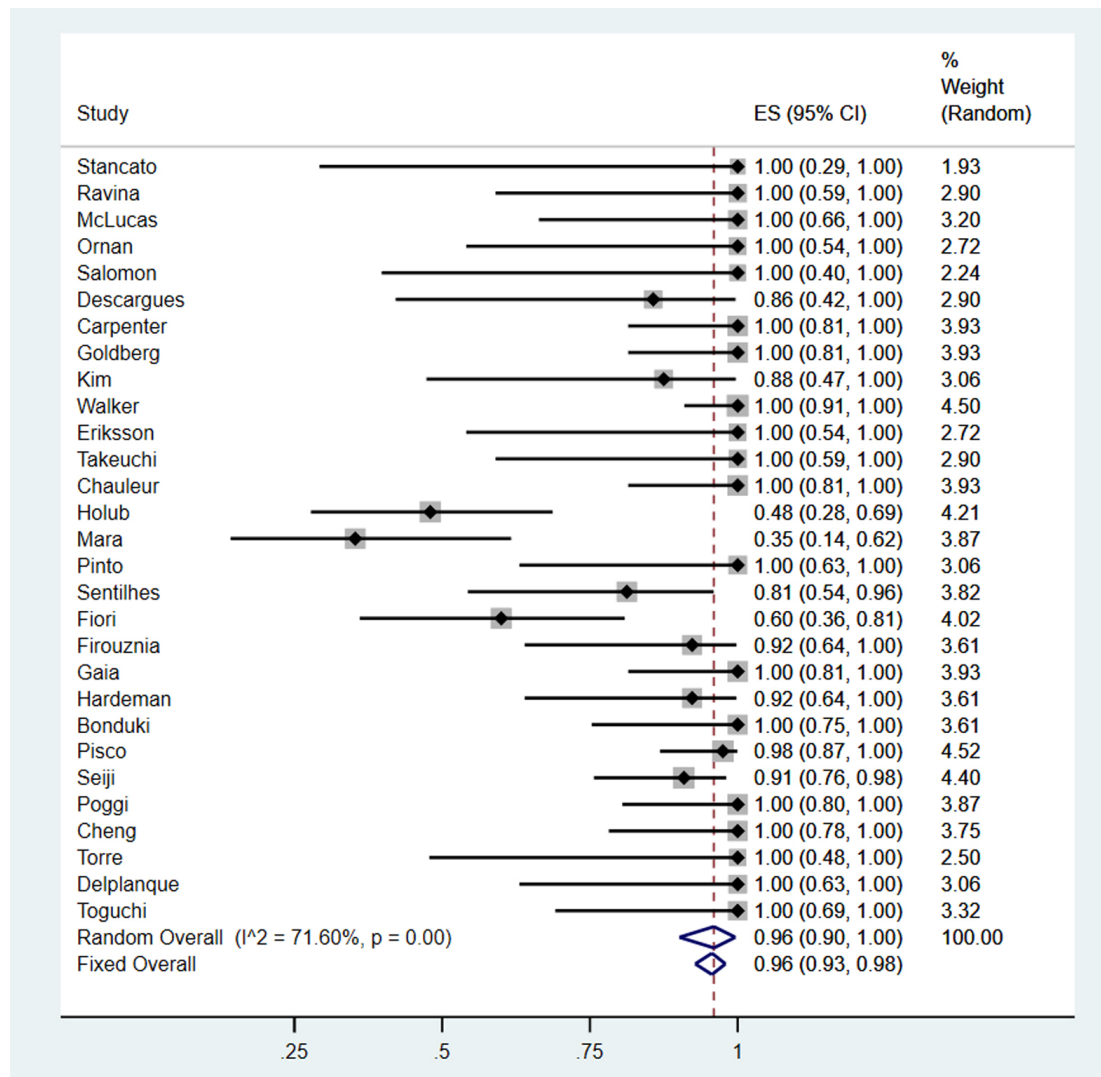


Fig. 2. Forest plots showing the total late-term pregnancy rate in women experiencing postpartum hemorrhage and symptomatic fibroids.

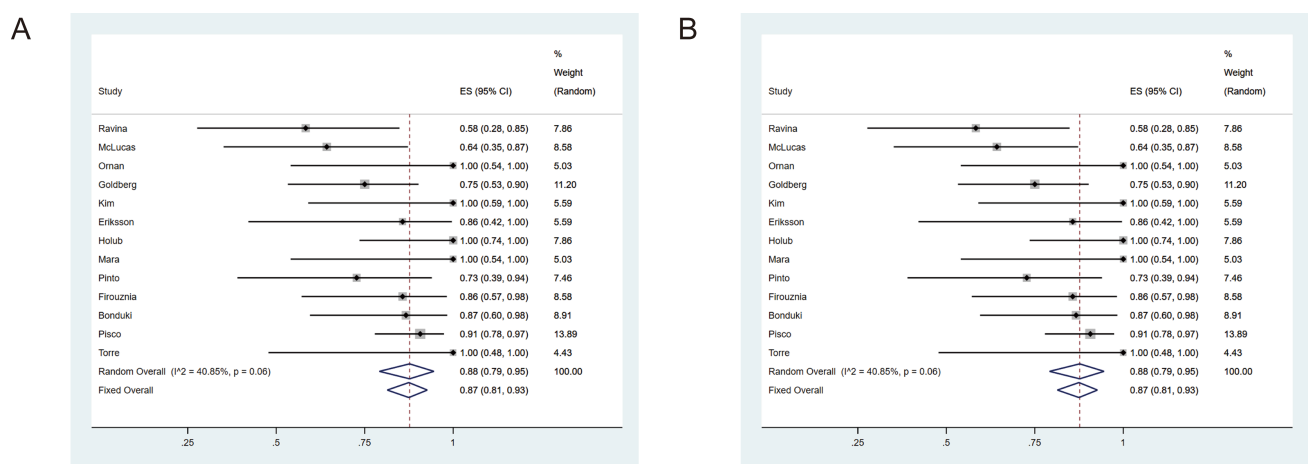


Fig. 3. Forest plots showing late-term pregnancy rate when treated by absorbable agents (A) or non-absorbable agents (B).

Table 1. The Included Studies in the Study.

Study	Age	Diagnosis	Embollic agent	Cases	Pregnancy	Miscarriages	Abortion/ ectopic	Pregnancy term ≥28 weeks	The rate of termed pregnancy (%)
Stancato [6]	20–44	obstetric hemorrhage	gelatin sponge pledget	17	3	0	0	3	100
Ravina [7]	23–43 (40)	leiomyomata	polyvinyl alcohol	12	12	5	0	7	58.33
McLucas [8]		leiomyomata	polyvinyl alcohol	400	14	5	0	9	64.28
Ornan [9]		postpartum hemorrhage	polyvinyl alcohol	28	6	0	0	6	100
Salomon [10]	23–45	post-partum haemorrhage		17	5	1	0	4	80
Descargues [11]		postpartum haemorrhage	gelatine sponge	27	10	3	1	6	66.67
Carpenter [12]		symptomatic fibroids		26	26	8		18	69.23
Goldberg [13]	18–59	Leiomyomata	polyvinyl alcohol particles	555	24	6		18	75
Kim [14]	20–40		polyvinyl alcohol particles	94	8	0	1	7	87.5
Walker [15]		leiomyomata		1200	56	17		39	69.64
Eriksson [16]		Massive postpartum hemorrhage	Gelfoam, metallic coils	20	7	1		6	85.71
Takeuchi [17]		hysteroscopic removal of a placental polyp	gelatin sponge	13	7	0		7	100
Chauleur [18]		primary post-partum hemorrhage		46	19	1		18	94.73
Holub [19]	32.3 ± 4.67	symptomatic fibroids	nonabsorptive Embosphere trisacryl gelatin particles	112	28	0	16	12	100
Mara [20]	32.2 ± 4.1	fibroid	Trisacryl gelatin microspheres	58	17	0	11	6	100
Pinto [21]	33–40	fibroid	tris-acryl gelatin microspheres	100	11	3	0	8	100
Sentilhes [22]		severe postpartum haemorrhage			16	0	3	13	100
Fiori [23]	20–43	postpartum hemorrhage		34	20	0	8	12	100
Firouznia [24]	35.7 ± 6.4	symptomatic fibroids	500-to710-microm polyvinyl alcohol particles	102	15	2	1	12	85.71
Gaia [25]	18–47	postpartum hemorrhage	absorbable gelatine sponge	113	19	1	0	18	94.73
Hardeman [26]	19–44	obstetrical hemorrhage	Absorbable materials	53	13	0	1	12	100
Bonduki [27]		symptomatic uterine fibroids	polyvinyl alcohol particles	187	15	2	0	13	86.67
Pisco [28]	36.0 ± 3.48	fibroid	Polyvinyl alcohol particles (PVA)	74	44	4	1	39	97.5
Seiji [29]		gelatin sponge		211	42	9	3	30	76.92
Poggi [30]	30.5 ± 5.5			103	17	0	0	17	100
Cheng [31]		postpartum hemorrhage		178	19	4	0	15	78.94
Torre [32]	≤40	symptomatic multiple fibroids	tris-acryl gelatin microspheres	15	5	0	0	5	100
Delplanque [33]				12	8	0	0	8	100
Toguchi [34]	34.1 ± 6.5	postpartum hemorrhage		23	14	4	0	10	71.43

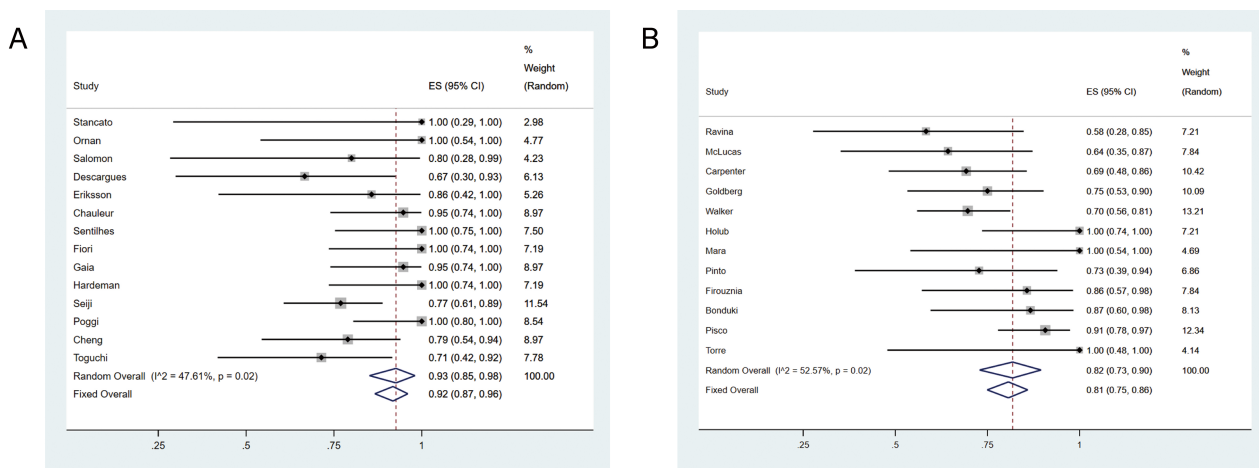


Fig. 4. Forest plot indicating the late-term pregnancy rate in UAE treatment due to obstetric hemorrhage (A) and symptomatic fibroids (B).

Twelve studies reported females that chose UAE for the treatment of symptomatic fibroids [7,8,12,13,15,19–21,24,27,28,32]. These 12 studies included 267 pregnancies, 52 early miscarriages, and 29 voluntary terminations; 186 pregnancies progressed to the late-term. Pooled data showed that the late-term pregnancy rate was 82% (95% CI, 73%–90%, $I^2 = 23.19$, $p = 0.02$) in a random model. We also identified heterogeneity ($p = 0.02$) between these studies (52.57%) (Fig. 4B).

4. Discussion

There are many concerns about the fertility of women following treatment with UAE. For example, a reduction in blood supply can result in atrophy of the uterine endometrium and abnormal fetal development in 2003, Tropeano *et al.* [35] reported permanent endometrial atrophy in a female with symptomatic fibroids who had been treated by UAE. In another study, Hayden performed a meta-analysis of pregnant females and reported an increased risk of miscarriage after UAE [5]. However, some positive results have also been reported after UAE. For example, Picone [36] reported that fetal growth and umbilical Doppler findings remained normal in the all of the observed cases after pelvic arterial embolization for postpartum hemorrhage. This report was very positive with regards to women who wish to achieve successful pregnancies after UAE treatment. UAE has now been performed for over thirty years, and continues to generate positive results in terms of subsequent pregnancies. However, the relative rate of late-term pregnancies is very diverse; the literature shows that this parameter varies from 58.33% to 100%. We performed this systematic review to provide an up-to-date synthesis of the published data relating to late-term pregnancies after UAE in women who wish to preserve their pregnancies.

Our meta-analysis revealed a high proportion of late-term pregnancies (96%; 95% CI, 90%–100%), although

heterogeneity was also evident in the pooled studies. Data showed that the proportion of late-term pregnancies in women who had received UAE were higher than the overall population. This may be due to more careful screening and examination, and also the desire to maintain pregnancies in women who have undergone UAE.

The embolic agents used for UAE can be divided into absorbable agents (e.g., gelatine sponge, Gelfoam) or non-absorbable agents (e.g., polyvinyl alcohol particles). Non-absorbable agents induce permanent embolization; this can potentially reduce the blood supply to the uterus. We divided UAE women into two groups, an absorbable agent group and a non-absorbable agent group. The late-term pregnancy rate was 92% (95% CI, 79%–100%) in the absorbable agent group and 88% (95% CI, 79%–95%) in the non-absorbable agent group. Consequently, it was evident that non-absorbable agents did not affect the fertility of women who received UAE.

There are some controversial results relating to pregnancy in women with fibroids. For example, Lee *et al.* [37] reviewed a series of pregnancies in women with fibroids and found that uterine fibroids are associated with an increased rate of negative pregnancy outcomes. However, Hartmann *et al.* [38] reported that women with fibroids are not associated with an increased risk of miscarriage; consequently, there is a clear need to carry out further investigations with regards to the effects of fibroids on pregnancies. In another paper, Homer *et al.* [5] observed an increased risk of miscarriage after UAE. In our current meta-analysis, the rate of late-term pregnancy was determined to be 93% (95% CI, 85%–93%) in patients who suffered postpartum haemorrhage and 82% (95% CI, 73%–90%) in patients with symptomatic fibroids. We were not able to compare rates between studies due to lack of randomization in such studies. However, it was evident that the rate of late-term pregnancy was lower in patients with symptomatic fibroids than in patients who experienced postpartum haemorrhage and

were treated with UAE. Recently, selective progesterone receptor modulators (SPRMs), for example, Ulipristal acetate (UPA), was also shown promising pregnancy results for the females with symptomatic fibroids [39]. However, because of shortage of records of these female enrolled in our study whether or not taken UPA, we couldn't compare with the pros and cons of the two kinds of treatments.

A successful pregnancy is associated with a range of patient-specific confounding factors, including maternal age, body mass index (BMI), maternal diseases, socioeconomic situations, and parity; these factors may exert independent effects on pregnancy outcomes [40]. Patients with symptomatic uterine fibroids are associated with endometrial atrophy following UAE [35]. However, once pregnancies have been successfully established, then there are good opportunities for a good outcome, as shown by our meta-analysis. When we pooled data from the studies used in our meta-analysis, we observed heterogeneity in terms of population demographics. We could not account for this heterogeneity in our statistical analysis. Despite these potential limitations, the high rate of successful pregnancies is impressive. Reassuringly, our data did not reveal any increased risk for preterm delivery, malpresentation, or IUGR, after UAE treatment.

5. Conclusions

Collectively, our data indicate that UAE is a beneficial technique but may also be counterproductive for the safety of late-term pregnancies. The results presented herein support the current recommendation that UAE should be considered as a relative contraindication for women who wish to retain their fertility [4].

Author Contributions

XZ and LL searched the literature, read the abstract of literature and collected the proper papers, drafted this manuscript, SL checked the literature and analyzed collective datasets, BY designed this study, revised the manuscript and provided finance support for this study. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

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