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The association of ultrafiltration with the outcomes of cardiopulmonary bypass surgery in adults with cardiovascular disease: The result of a systematic review and meta-analysis

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Abstract

Introduction: Previous studies have shown that ultrafiltration (UF) is associated with improved minor and major outcomes of cardiopulmonary bypass (CPB) by improving tissue perfusion as well as lowering the patient's hematocrit and blood loss and finally reducing the mortality. This meta-analysis aimed to pool the data of the previous studies on the association between using UF in the perioperative period and clinical outcomes in adult patients undergoing CPB.

Methods: We searched Ovid MEDLINE, Ovid Embase Scopus, Web of Science, Google Scholar, and EBSCO CINAHL from inception up to June 29th, 2019. The studies that assessed the association of UF with the outcomes of CPB in adults were eligible for inclusion. We did not restrict the search to time or language. Two independent investigators screened the identified studies and extracted the data in duplicate. We analyzed sixteen different clinical outcomes. Heterogeneity was assessed using Cochrane collaboration tools.

Results: Primary search identified 1114 studies from which 22 studies with 8538 patients were found eligible for inclusion. Results showed a statistically significant reduction in perioperative bleeding (-107.59 (ml) CI [-179.01, -36.18]), red blood cell transfusion (-0.76 (unit/patient) CI [-1.02,-0.51]) and ICU length of stay (-0.16 (day) CI [-0.31,-0.01]) in the group with UF compared to the control group. Aortic cross-clamp time, CPB time, ventilation time, hospital length of stay, as well as number of myocardial infarctions, chest infection, perioperative arrhythmia, low cardiac output, stroke/TIA, acute renal failure, intra-aortic balloon pump, reoperation and mortality was not statistically different between the two groups (p=>0.05).

Conclusion: Using UF in adult patients undergoing CPB is associated with reduced perioperative bleeding, red blood cell transfusion, and ICU length of stay. However, the use of UF was not associated with the reduction of major cardiovascular outcomes.

Introduction

Cardiopulmonary bypass (CPB) contributes to hemodilution, coagulation abnormalities, activation of inflammatory mediators, and as a result end-organ dysfunction in cardiac surgery [1]. This hemodilution occurs due to the use of priming solution that fills the circuit before perfusion begins, it can be further exacerbated using cardioplegia solution. Once CPD is discontinues this hemodiluted blood remain in the extracorporeal circuit and is slowly transfused back to the patient during or after aortic decannulation.

This hemodilution after CBP can be reversed or reduced by Ultrafiltration (UF), in which cell-free fluid is removed from the circulation. Utilizing a semipermeable membrane that allow for the transfer of water, electrolytes, and small molecules (on average up to 20 kDa) which may reduce transfusion requirements, inflammatory mediators [2] and improve hypercoagulability, post bypass hemodynamics and end-organ perfusion [3,4]. Excess removal of circulating volume has been linked to induce renal dysfunction in UF [5]. The two main forms of UF are conventional UF (CUF) which is run during CBP and cannot run following its discontinuation. In contrast, modified UF (MUF) is performed after completion of CBP, utilizing the aortic cannula.

In the pediatric population UF has been established as standard of care after CBP given its pronounced benefits [6]. Several randomized

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trials have tried to establish the effect of UF in adult undergoing cardiac surgery. All these studies had an intervention and control group, mortality, and other surrogate endpoints like ICU length of stay, cardiovascular events, acute kidney injury, and transfusion requirements were studied. The aim of this study is to evaluate the existing evidence on the use of UF, (whether CUF or MUF) in adults that undergoing CBP and its possible benefits.

Methods

Data source and study selection

This meta-analysis was conducted using a preplanned protocol. All results were reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. With the assistance of an expert librarian, Ovid MEDLINE, Ovid, Embase, Scopus, Web of Science, Google Scholar, and EBSCO CINAHL were searched from their inception up to June 29th, 2019. The search was not restricted to time, publication status or language. All relevant references and Authors' (of the included studies) related publication hand-searched for relevant studies. Medical Subject Headings (MeSH) terms were used with keywords for UF, cardiac surgery, and adult. We included randomized and quasi-randomized designs, pre-post trials, cross-sectional studies, and observational studies. Only studies on using UF in adult patients undergoing CBP and have a control group were included in the meta-analysis without restriction to the type of cardiac surgery.

Studies search and selection is illustrated in (Figure 1). Our primary search identified 1559 potentially eligible studies. Duplicates were excluded and 1114 studies were included for screening, each title and abstract were evaluated by two reviewers independently using a systematic review software (Covidence, London, UK), 45 publications were retrieved, and their manuscripts were evaluated for possible inclusion. A total of 22 studies met all eligibility criteria and were included in our meta-analysis after the agreement of the two reviewers.

Data extraction and analysis

Data extraction was done by two independent reviewers with discrepancies resolved by consensus. Data included: first author, date of publishing, methods, risk of bias assessment, participants, intervention and control groups, and results (dichotomous or continuous outcomes).

In addition to the primary end point of perioperative bleed, PRBC transfusion, ICU length of stay, the following clinical parameters were collected: average aorta cross-clamp (ACC) time, average CPB time, ventilation time, hospital length of stay, myocardial infarction, Pulmonary complications, perioperative arrhythmia, low cardiac output, stroke/TIA, acute renal failure, the use of intra-aortic balloon pump, reoperation and mortality.

The meta-analysis was performed using Review Manager, version 5 (Cochrane Collaboration). Mean differences were evaluated along with 95% confidence intervals (95% CIs). All parameters were summarized using the random-effects model. Heterogeneity was tested using I2 index for each outcome. Risk of bias was assessed using Cochrane collaboration tools.

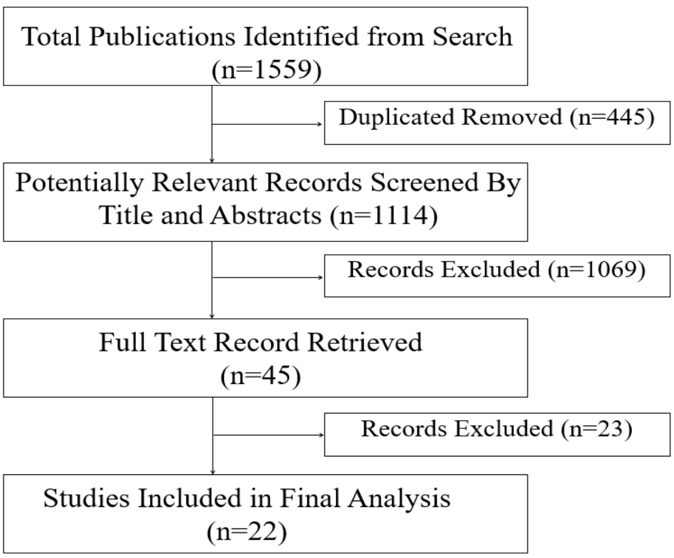

Figure 1. PRISMA flowchart describing the study's systematic literature search and study selection

Results

We included 22 observational studies in our analysis, baseline characters are presented in (Table 1) [1,5,7-26]. In the intervention group there was a statistically significant reduction in in postoperative bleeding (ml) (-107.59 CI [-179.01, -36.18]), postoperative blood transfusion (unit/pt) (-0.76 CI [-1.02,0.51]) and ICU length of stay (-0.16 CI [-0.31,0.01]). There were no statistically significant differences between both groups in average ACC time is (-0.69 CI [-0.2,0.62]), average CPB time (-0.85 CI [-1087,0.16]), ventilation time (-0.86 CI [-3.08,1.37]), hospital length of stay (-0.41 CI [-1.0,0.18]), mortality (0.94 CI [0.65,1.37]), myocardial infarction (0.62 CI [0.33,1.16]), chest infection (-0.69 CI [0.25,1.15]), perioperative arrhythmia (1.23 CI [0.81,1.85]), low cardiac output (0.92 CI [0.43,1.95]), stroke/ Transient Ischemic Attack (TIA) (0.85 CI [0.56,1.29]), acute renal failure (1.1 CI [0.81,1.49]), intra-aortic balloon pump (0.75 CI [0.24,2.36]), and reoperation (0.99 CI [0.65,1.5]).

Discussion

This was the first systematic review and meta-analysis about this subject. We included 22 studies evaluating the utility of UF in adult undergoing cardiac surgery. Among the studies included, sixteen different outcomes were analyzed including mortality. In this systematic analysis the only endpoints that demonstrated a statistically significant difference were post-operative bleeding, transfusion of RBCs and length of stay in the ICU. There was no evidence of mortality benefit which corroborates every single study included in this analysis.

The results of the present study showed that UF is associated with decrease in post-operative bleeding, transfusion of RBCs and length of stay in the ICU but not with major cardiovascular outcomes.

Ultrafiltration have shown to improve postoperative hemodynamics and myocardial recovery as well as cerebral and hemostatic function in pediatric cardiac surgery [27], with these benefits UF has been adapted as the standard of care in this population. The value of UF in adult cardiac surgery has not been thoroughly explored. We conducted this meta-analysis to better evaluate the utility of UF, Both MUF and CUF in adult (Figure 2-17).

The main benefit that has been consistent with the use of UF is a decrease in transfusion requirements. Multiple studies have demonstrated that these appears to be driven by correcting hemodilution and less post-operative bleeding. Our study found a statistically significant decrease in post-operative bleeding. This was

Table 1. Demographic data of the studies±

Study	Number of participants		Number of participants	Male (%)	CABG (%)	Age (±SD)
Babka 1997	60	Intervention	30	70	100	63(±9)
		Control	30	87	100	59(±11)
Blanchard 2000	26	Intervention	13	69	100	66
		Control	13	69	100	66
Boga 2000	40	Intervention	20	80	100	58(±11)
		Control	20	70	100	61(±8)
Boodhwani 2009	65	Intervention	29	66		66(±13)
		Control	36	78		71(±10)
Coskun 2013	46	Intervention	26	89	89	58(±7)
		Control	20	70	80	58(±11)
De Baar 2003	60	Intervention	29	79	100	66(±9)
		Control	31	74	100	67(±8)
El-Tahan 2010	60	Intervention	30	60		28
		Control	30	70		27
Kiziltepe 2001	40	Intervention	20	65	75	60(±14)
		Control	20	70	75	60(±8)
Luciani 2001	573	Intervention	284	66	57	64(±11)
		Control	289	74	60	63(±14)
Matata 2015	199	Intervention	97	59	31	76
		Control	102	60	30	73
Oliver 2004	127	Intervention	64	84	44	62(±1)
		Control	63	83	57	62(±12)
Papadopolous 2013	50	Intervention	25	52		74(±6)
		Control	25	64		75(±5)
Paugh 2015	6407	Intervention	1362	75		
		Control	5045	75		
Soliman 2016	283	Intervention	138	50	53	60(±12)
		Control	145	42	47	60(±12)
Zhang 2009	94	Intervention	47			
		Control	47			
Naveed 2015	80	Intervention	40	72	16	47(±13)
		Control	40	82	24	51(±9)
Torina 2012	60	Intervention	30	80	100	55(±7)
		Control	30	93	100	56(±9)
Grunenfelder 2000	50	Intervention	30		100	
		Control	20		100	
Tollman 2002	30	Intervention	15	66		63(±9)
		Control	15	80		63(±7)
Raman 2003	118	Intervention	61	66	39	68(±12)
		Control	57	77	35	65(±13)
Steffens 2008	30	Intervention	15	90		58(±11)
		Control	15	66		58(±16)
Kosour 2016	40	Intervention	20	64	100	59(±10)
		Control	20	75	100	60(±10)

driven by two of the studies [11,13] that reported a decrease in mean post-operative bleeding of 200 to 250mL. Three other studies have demonstrated a trend towards less post-operative bleeding without reaching statistical significance [14,22,23]. This decrease in bleeding was likely one of the main contributors to the reduction on transfusion requirements of 0.76 units/patient (95% CI: -1.02, -0.51), which is also explained by the reduction in hemodilution after CBP, at least 6 of the studies included demonstrated a significant decrease in units transfused or at least a trend towards significance.

Nine Studies which reported mortality as an endpoint were included. In a multicenter, observational cohort study which assessed the effect of UF (CUF) versus control group [5], there was no significant difference in mortality rate between patients who have received CUF and those who have not. A result which has been consistent among all the manuscripts included. On the other hand, Paugh et al. [5] did found differences in morbidity, mainly rates of acute kidney injury which were greater in the CUF group (adjusted OR 1.36; 95% confidence interval, 1.12 to 1.65; p = 0.002).

The risk of acute kidney injury (AKI) is of great interest when studying UF. Several mechanisms can contribute to AKI; both fluid overload as a result of CBP as well as excessive fluid removal during UF can potentially impact renal function. Our results demonstrate no significant impact of UF on renal function. All 6 studies which investigated AKI after filtration did not demonstrate a clear benefit or harm of using UF. Paugh et al. [5] demonstrated an increased risk of developing AKI after CPB and UF which appeared to be mainly related to increasing volume of UF in patients with baseline chronic kidney injury. This might be explained by the excessive risk of developing AKI

Study or Subgroup	HF Mean	HF SD	HF Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Babka 1997	32	12	30	38	15	30	3.7%	-6.00 [-12.87, 0.87]
Blanchard 2000	55	7.63	13	59	7.63	13	5.0%	-4.00 [-9.87, 1.87]
Boga 2000	53	15.07	20	48.75	16.72	20	1.8%	4.25 [-5.61, 14.11]
Boodhwani 2009	65	23	29	67	21	36	1.5%	-2.00 [-12.82, 8.82]
Coşkun 2013	62.3	20.2	26	54.8	25.3	20	0.9%	7.50 [-6.04, 21.04]
de Baar 2013	85	26	29	86	25	31	1.0%	-1.00 [-13.92, 11.92]
El-Tahan 2010	57.5	25.1	30	60.2	28.8	30	0.9%	-2.70 [-16.37, 10.97]
Kiziltepe 2001	62.8	14.5	20	63.8	18.2	20	1.7%	-1.00 [-11.20, 9.20]
Kosour 2016	49	11.6	20	45.5	10.9	20	3.6%	3.50 [-3.48, 10.48]
Luciani 2001	67.36	32.5	284	63.36	30.3	289	6.5%	4.00 [-1.15, 9.15]
Matata 2015	76	45	97	80	49	102	1.0%	-4.00 [-17.06, 9.06]
Oliver 2004	43.8	19.5	64	42.8	16	63	4.5%	1.00 [-5.20, 7.20]
Papadopoulos 2013	109	32	25	113	34	25	0.5%	-4.00 [-22.30, 14.30]
Paugh 2015	73.2	31.6	1362	74.8	31.8	5045	48.3%	-1.60 [-3.49, 0.29]
Soliman 2016	99.36	13.79	138	99.31	13.3	145	17.4%	0.05 [-3.11, 3.21]
Zhang 2009	83.7	27.4	60	80.4	29.2	60	1.7%	3.30 [-6.83, 13.43]
Total (95% CI)			**2247**			**5949**	**100.0%**	**-0.69 [-2.01, 0.62]**

Heterogeneity: Tau² = 0.00; Chi² = 12.96, df = 15 (P = 0.61); I² = 0%
Test for overall effect: Z = 1.03 (P = 0.30)

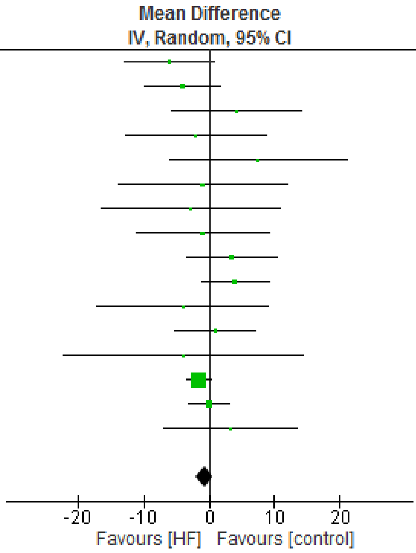

Figure 2. The results of meta-analysis on the association of Ultrafiltration and the average aorta cross-clamp (ACC) time in minutes

Study or Subgroup	HF Mean	HF SD	HF Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Babka 1997	64	21	30	73	21	30	0.9%	-9.00 [-19.63, 1.63]
Blanchard 2000	112	1.665	13	113	1.665	13	63.1%	-1.00 [-2.28, 0.28]
Boga 2000	74.1	19.2	20	71.3	16.4	20	0.8%	2.80 [-8.27, 13.87]
Coşkun 2013	94.4	44.7	26	96.8	36.3	20	0.2%	-2.40 [-25.82, 21.02]
El-Tahan 2010	102.4	20.5	30	110.1	27.3	30	0.7%	-7.70 [-19.92, 4.52]
Kiziltepe 2001	101.9	18.3	20	98.5	25.6	20	0.5%	3.40 [-10.39, 17.19]
Kosour 2016	72.4	18.9	20	74.85	17.6	20	0.8%	-2.45 [-13.77, 8.87]
Luciani 2001	111.36	39.2	284	108.76	40.6	289	2.4%	2.60 [-3.93, 9.13]
Matata 2015	110	62	97	109	56	102	0.4%	1.00 [-15.44, 17.44]
Naveed 2015	117.37	38.78	40	120.62	20.97	40	0.6%	-3.25 [-16.91, 10.41]
Oliver 2004	67.3	29.9	64	66.4	27.2	63	1.0%	0.90 [-9.04, 10.84]
Papadopoulos 2013	146	50	25	160	63	25	0.1%	-14.00 [-45.53, 17.53]
Paugh 2015	96.1	42	1362	96	39	5045	16.8%	0.10 [-2.38, 2.58]
Soliman 2016	115.34	17.21	138	114.32	17.63	145	6.3%	1.02 [-3.04, 5.08]
Torina 2012	51	10	30	56	8	30	4.9%	-5.00 [-9.58, -0.42]
Zhang 2009	120.2	40.5	60	116.6	46.8	60	0.4%	3.60 [-12.06, 19.26]
Total (95% CI)			**2259**			**5952**	**100.0%**	**-0.85 [-1.87, 0.16]**

Heterogeneity: Tau² = 0.00; Chi² = 11.26, df = 15 (P = 0.73); I² = 0%
Test for overall effect: Z = 1.65 (P = 0.10)

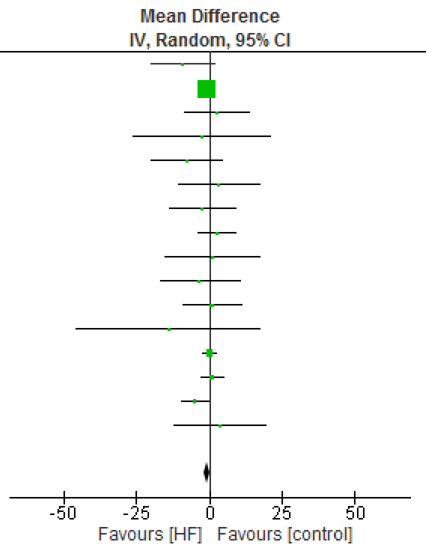

Figure 3. The results of meta-analysis on the association of Ultrafiltration and the average cardiopulmonary bypass (CPB) time in minutes

Study or Subgroup	HF Mean [hr]	HF SD [hr]	HF Total	Control Mean [hr]	Control SD [hr]	Control Total	Weight	Mean Difference IV, Random, 95% CI [hr]
Coşkun 2013	14	5	26	12.7	7	20	9.1%	1.30 [-2.32, 4.92]
de Baar 2013	17	3.6	29	23.3	21	31	5.1%	-6.30 [-13.81, 1.21]
El-Tahan 2010	5.5	2.41	30	8.6	6.21	30	10.5%	-3.10 [-5.48, -0.72]
GruÈnenfelder 1999	15.4	9.2749	60	14.873	4.6876	37	10.1%	0.53 [-2.26, 3.32]
Kiziltepe 2001	11.9	4.1	20	14.1	12.9	20	6.5%	-2.20 [-8.13, 3.73]
Kosour 2016	6	3.52	20	4	1.76	20	11.2%	2.00 [0.28, 3.72]
Luciani 2001	22.56	41.3	284	27.66	64	289	4.2%	-5.10 [-13.90, 3.70]
Matata 2015	12	11	97	9	8	102	10.2%	3.00 [0.32, 5.68]
Oliver 2004	8.016	5.14	64	10.3	6.75	63	10.8%	-2.28 [-4.37, -0.19]
Tallman 2002	10.23	3.94	15	8.34	2.29	15	10.6%	1.89 [-0.42, 4.20]
Zhang 2009	14.35	1.66	60	18.64	1.57	60	11.9%	-4.29 [-4.87, -3.71]
Total (95% CI)			**705**			**687**	**100.0%**	**-0.86 [-3.08, 1.37]**

Heterogeneity: Tau² = 10.79; Chi² = 100.75, df = 10 (P < 0.00001); I² = 90%
Test for overall effect: Z = 0.75 (P = 0.45)

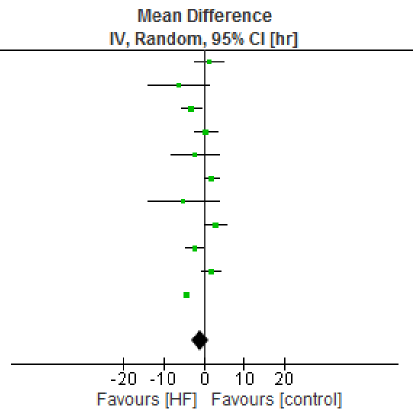

Figure 4. The results of meta-analysis on the association of Ultrafiltration and the ventilation time in hours

Study or Subgroup	HF Mean	HF SD	HF Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Babka 1997	440	192	30	451	136	30	18.5%	-11.00 [-95.19, 73.19]
Blanchard 2000	720	193.1	13	770	193.1	13	12.0%	-50.00 [-198.45, 98.45]
El-Tahan 2010	808	137.42	30	1,064	337.13	30	13.6%	-256.00 [-386.28, -125.72]
GruÈnenfelder 1999	1,100	400	30	1,130	250	20	9.6%	-30.00 [-210.26, 150.26]
GruÈnenfelder-A 1999	1,140	370	30	1,450	633	17	4.0%	-310.00 [-638.74, 18.74]
Kiziltepe 2001	522.2	233.4	20	740	198.4	20	13.2%	-217.80 [-352.05, -83.55]
Luciani 2001	542.46	300	284	599.56	471.3	289	20.6%	-57.10 [-121.67, 7.47]
Tallman 2002	917.67	160.62	15	1,023.33	358.09	15	8.5%	-105.66 [-304.27, 92.95]
Total (95% CI)			**452**			**434**	**100.0%**	**-107.59 [-179.01, -36.18]**

Heterogeneity: Tau² = 5345.41; Chi² = 16.47, df = 7 (P = 0.02); I² = 58%
Test for overall effect: Z = 2.95 (P = 0.003)

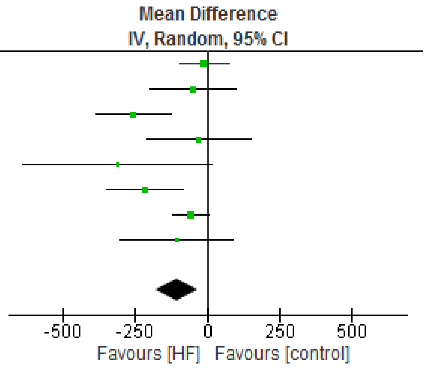

Figure 5. The results of meta-analysis on the association of Ultrafiltration and the perioperative bleed (ml)

Study or Subgroup	HF Mean	HF SD	HF Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Babka 1997	0.6	1.3	30	0.75	1.5	30	7.2%	-0.15 [-0.86, 0.56]
Boga 2000	0.83	0.27	20	1.84	0.31	20	15.2%	-1.01 [-1.19, -0.83]
Boodhwani 2009	2	1.73	29	2.6	4.3	36	2.3%	-0.60 [-2.14, 0.94]
Coşkun 2013	1.8	1.2	26	2.6	1.3	20	7.0%	-0.80 [-1.53, -0.07]
El-Tahan 2010	2.8	0.82	30	4.4	1.32	30	9.2%	-1.60 [-2.16, -1.04]
GruÈnenfelder 1999	1.2	1.1	30	1.4	1.3	20	7.4%	-0.20 [-0.89, 0.49]
GruÈnenfelder-A 1999	1.4	1.5	30	1.5	1.1	17	6.8%	-0.10 [-0.85, 0.65]
Luciani 2001	1.66	2.6	284	2.25	3.8	289	9.6%	-0.59 [-1.12, -0.06]
Raman 2003	0.62	2.66	61	0.72	2.66	57	4.9%	-0.10 [-1.06, 0.86]
Soliman 2016	1.55	0.28	138	2.78	0.78	145	15.7%	-1.23 [-1.37, -1.09]
Steffens 2008	0.1	0.32	10	0.67	1.41	9	5.1%	-0.57 [-1.51, 0.37]
Torina 2012	0.7	0.7	30	1.5	1.3	30	9.6%	-0.80 [-1.33, -0.27]
Total (95% CI)			**718**			**703**	**100.0%**	**-0.76 [-1.02, -0.51]**

Heterogeneity: Tau² = 0.10; Chi² = 38.13, df = 11 (P < 0.0001); I² = 71%
Test for overall effect: Z = 5.87 (P < 0.00001)

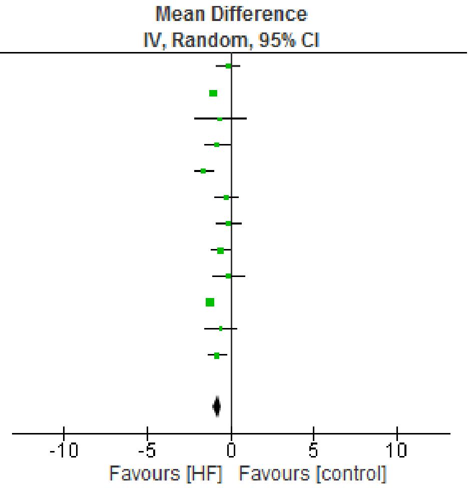

Figure 6. The results of meta-analysis on the association of Ultrafiltration and the red blood cells transfusion (unit/patient)

Study or Subgroup	HF Mean	HF SD	HF Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Coşkun 2013	2.33	1.16	26	3.96	3.875	20	0.7%	-1.63 [-3.39, 0.13]
El-Tahan 2010	4.1	1.61	30	7.6	3.91	30	1.0%	-3.50 [-5.01, -1.99]
GruÈnenfelder 1999	2	1.9	30	2.2	3.3	20	0.9%	-0.20 [-1.80, 1.40]
GruÈnenfelder-A 1999	2.4	1.9	30	2.4	2.3	17	1.3%	0.00 [-1.29, 1.29]
Kiziltepe 2001	2.05	0.23	20	2.3	1.34	20	4.8%	-0.25 [-0.85, 0.35]
Kosour 2016	1.58	0.125	20	1.5	0.08	20	17.2%	0.08 [0.01, 0.15]
Luciani 2001	1.66	2.05	284	1.93	3.03	289	7.5%	-0.27 [-0.69, 0.15]
Naveed 2015	1.89	0.91	40	2.2	0.93	40	7.9%	-0.31 [-0.71, 0.09]
Oliver 2004	1.03	0.39	64	1	0.36	63	15.7%	0.03 [-0.10, 0.16]
Papadopoulos 2013	5.1	6.45	25	5.7	9.21	25	0.1%	-0.60 [-5.01, 3.81]
Tallman 2002	0.91	0.176	15	0.96	0.19	15	15.7%	-0.05 [-0.18, 0.08]
Torina 2012	3.4	0.3	30	3.5	0.3	30	15.1%	-0.10 [-0.25, 0.05]
Zhang 2009	3.11	0.71	60	3.53	0.63	60	12.3%	-0.42 [-0.66, -0.18]
Total (95% CI)			**674**			**649**	**100.0%**	**-0.16 [-0.31, -0.01]**

Heterogeneity: Tau² = 0.03; Chi² = 48.49, df = 12 (P < 0.00001); I² = 75%
Test for overall effect: Z = 2.07 (P = 0.04)

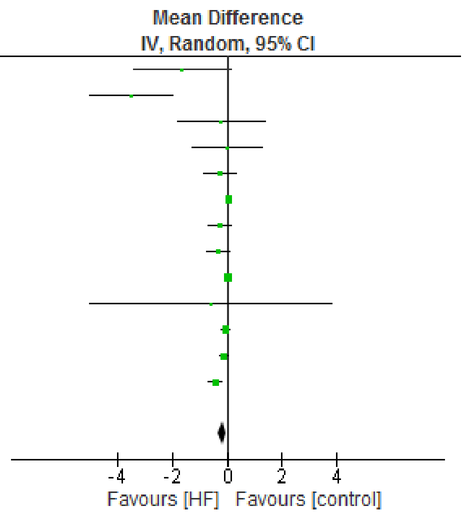

Figure 7. The results of meta-analysis on the association of Ultrafiltration and the ICU length of stay (days)

Study or Subgroup	HF Mean	HF SD	HF Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Babka 1997	6.4	1.5	30	6.4	2.1	30	12.8%	0.00 [-0.92, 0.92]
Blanchard 2000	13	2.74	13	12	2.74	13	5.5%	1.00 [-1.11, 3.11]
Boodhwani 2009	8.9	5.6	29	9.6	9.8	36	2.1%	-0.70 [-4.50, 3.10]
Coşkun 2013	5.5	1.4	26	8.1	3.4	20	7.9%	-2.60 [-4.18, -1.02]
El-Tahan 2010	10.4	2.11	30	18.7	10.6	30	2.1%	-8.30 [-12.17, -4.43]
GruÈnenfelder 1999	11	2.1	30	10.4	4.3	20	5.8%	0.60 [-1.43, 2.63]
GruÈnenfelder-A 1999	9.5	2.9	30	10.8	4	17	5.3%	-1.30 [-3.47, 0.87]
Kiziltepe 2001	7.5	1.1	20	7.7	2.3	20	11.2%	-0.20 [-1.32, 0.92]
Luciani 2001	8.56	15.3	284	10.16	33.8	289	1.7%	-1.60 [-5.88, 2.68]
Matata 2015	10	9	97	10	9	102	4.3%	0.00 [-2.50, 2.50]
Papadopoulos 2013	13.4	9.27	25	12.2	6.5	25	1.6%	1.20 [-3.24, 5.64]
Tallman 2002	3.82	0.77	15	3.62	0.52	15	16.7%	0.20 [-0.27, 0.67]
Torina 2012	5.1	0.5	30	4.9	0.5	30	18.1%	0.20 [-0.05, 0.45]
Zhang 2009	15.79	7.11	60	17.45	5.64	60	4.9%	-1.66 [-3.96, 0.64]
Total (95% CI)			**719**			**707**	**100.0%**	**-0.41 [-1.00, 0.18]**

Heterogeneity: Tau² = 0.48; Chi² = 36.16, df = 13 (P = 0.0006); I² = 64%
Test for overall effect: Z = 1.37 (P = 0.17)

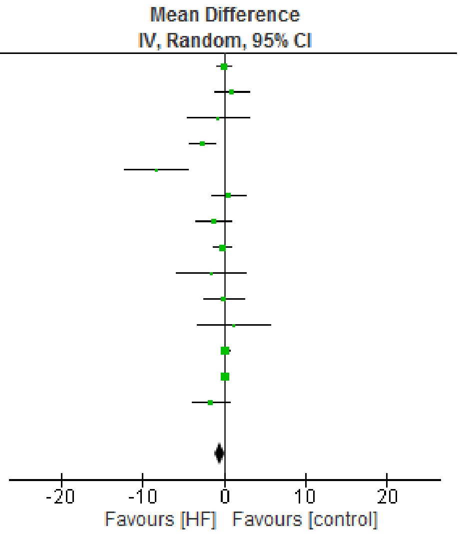

Figure 8. The results of meta-analysis on the association of Ultrafiltration and the hospital length of stay (days)

Study or Subgroup	HF Events	HF Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
Coşkun 2013	1	26	1	20	1.7%	0.76 [0.04, 12.95]
El-Tahan 2010	1	30	2	30	2.3%	0.48 [0.04, 5.63]
Luciani 2001	7	284	11	289	14.9%	0.64 [0.24, 1.67]
Matata 2015	3	97	10	102	7.9%	0.29 [0.08, 1.10]
Naveed 2015	1	40	3	40	2.6%	0.32 [0.03, 3.18]
Papadopoulos 2013	1	25	2	25	2.3%	0.48 [0.04, 5.65]
Paugh 2015	22	1362	60	5045	56.8%	1.36 [0.83, 2.23]
Raman 2003	7	61	6	57	10.3%	1.10 [0.35, 3.50]
Zhang 2009	0	60	1	60	1.3%	0.33 [0.01, 8.21]
Total (95% CI)		**1985**		**5668**	**100.0%**	**0.94 [0.65, 1.37]**
Total events	43		96			

Heterogeneity: Tau² = 0.00; Chi² = 7.79, df = 8 (P = 0.45); I² = 0%
Test for overall effect: Z = 0.31 (P = 0.75)

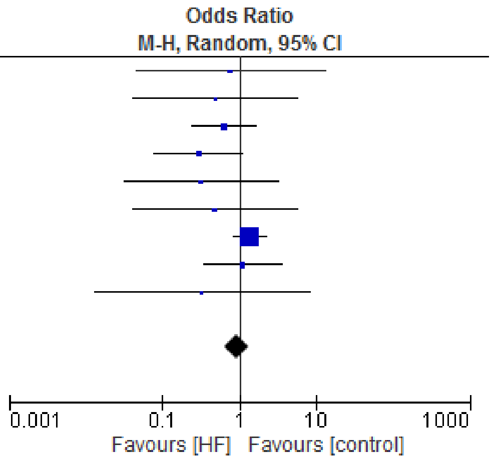

Figure 9. The results of meta-analysis on the association of Ultrafiltration and mortality

Study or Subgroup	HF Events	HF Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
Kiziltepe 2001	0	20	2	20	4.1%	0.18 [0.01, 4.01]
Luciani 2001	15	284	21	289	84.5%	0.71 [0.36, 1.41]
Matata 2015	1	97	3	102	7.6%	0.34 [0.04, 3.36]
Zhang 2009	0	60	1	60	3.8%	0.33 [0.01, 8.21]
Total (95% CI)		**461**		**471**	**100.0%**	**0.62 [0.33, 1.16]**
Total events	16		27			

Heterogeneity: Tau² = 0.00; Chi² = 1.18, df = 3 (P = 0.76); I² = 0%
Test for overall effect: Z = 1.50 (P = 0.13)

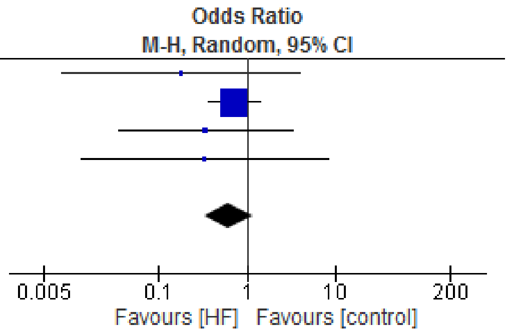

Figure 10. The results of meta-analysis on the association of Ultrafiltration and the incidence of myocardial infarction

Study or Subgroup	HF Events	HF Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
GruÈnenfelder 1999	8	30	3	20	15.9%	2.06 [0.47, 8.96]
GruÈnenfelder-A 1999	4	30	7	17	16.4%	0.22 [0.05, 0.92]
Luciani 2001	4	284	2	289	13.2%	2.05 [0.37, 11.28]
Matata 2015	7	97	22	102	25.3%	0.28 [0.11, 0.70]
Raman 2003	8	61	15	57	24.4%	0.42 [0.16, 1.09]
Zhang 2009	0	60	1	60	4.9%	0.33 [0.01, 8.21]
Total (95% CI)		**562**		**545**	**100.0%**	**0.54 [0.25, 1.15]**
Total events	31		50			

Heterogeneity: Tau² = 0.38; Chi² = 9.16, df = 5 (P = 0.10); I² = 45%
Test for overall effect: Z = 1.61 (P = 0.11)

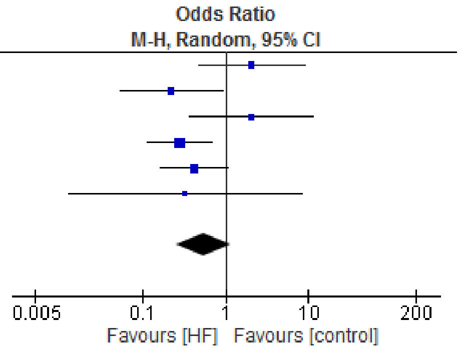

Figure 11. The results of meta-analysis on the association of Ultrafiltration and the chest infection incidence

Study or Subgroup	HF Events	HF Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
Babka 1997	8	30	6	30	11.6%	1.45 [0.44, 4.86]
Coşkun 2013	1	26	1	20	2.1%	0.76 [0.04, 12.95]
GruÈnenfelder 1999	15	30	9	20	13.1%	1.22 [0.39, 3.80]
GruÈnenfelder-A 1999	15	30	8	17	11.9%	1.13 [0.34, 3.70]
Luciani 2001	2	284	1	289	2.9%	2.04 [0.18, 22.65]
Matata 2015	58	97	57	102	53.3%	1.17 [0.67, 2.06]
Zhang 2009	3	60	2	60	5.1%	1.53 [0.25, 9.48]
Total (95% CI)		**557**		**538**	**100.0%**	**1.23 [0.81, 1.85]**
Total events	102		84			

Heterogeneity: Tau² = 0.00; Chi² = 0.46, df = 6 (P = 1.00); I² = 0%
Test for overall effect: Z = 0.98 (P = 0.33)

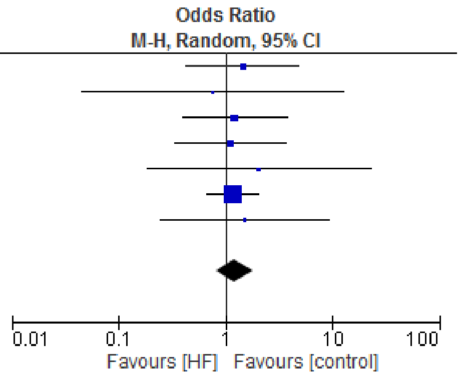

Figure 12. The results of meta-analysis on the association of Ultrafiltration and the perioperative arrhythmia

Study or Subgroup	HF Events	HF Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
Kiziltepe 2001	4	20	4	20	13.9%	1.00 [0.21, 4.71]
Luciani 2001	9	284	13	289	23.5%	0.69 [0.29, 1.65]
Matata 2015	6	97	11	102	20.7%	0.55 [0.19, 1.54]
Paugh 2015	261	1362	555	5045	33.6%	1.92 [1.63, 2.25]
Zhang 2009	1	60	3	60	8.2%	0.32 [0.03, 3.19]
Total (95% CI)		**1823**		**5516**	**100.0%**	**0.92 [0.43, 1.95]**
Total events	281		586			

Heterogeneity: Tau² = 0.43; Chi² = 13.06, df = 4 (P = 0.01); I² = 69%
Test for overall effect: Z = 0.22 (P = 0.82)

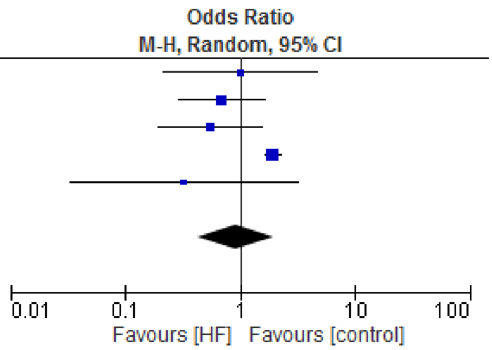

Figure 13. The results of meta-analysis on the association of Ultrafiltration and the low cardiac output

Study or Subgroup	HF Events	HF Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
Coşkun 2013	0	26	1	20	1.7%	0.25 [0.01, 6.35]
Kiziltepe 2001	1	20	2	20	2.9%	0.47 [0.04, 5.69]
Luciani 2001	3	284	6	289	9.1%	0.50 [0.12, 2.03]
Paugh 2015	22	1362	76	5045	77.8%	1.07 [0.67, 1.73]
Raman 2003	2	61	6	57	6.6%	0.29 [0.06, 1.49]
Zhang 2009	0	60	2	60	1.9%	0.19 [0.01, 4.11]
Total (95% CI)		**1813**		**5491**	**100.0%**	**0.85 [0.56, 1.29]**
Total events	28		93			

Heterogeneity: Tau² = 0.00; Chi² = 4.82, df = 5 (P = 0.44); I² = 0%
Test for overall effect: Z = 0.77 (P = 0.44)

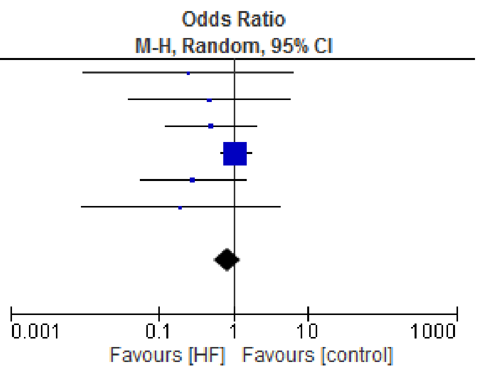

Figure 14. The results of meta-analysis on the association of Ultrafiltration and the stroke/TIA

Study or Subgroup	HF Events	HF Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
El-Tahan 2010	0	30	1	30	0.9%	0.32 [0.01, 8.24]
Luciani 2001	5	284	8	289	6.6%	0.63 [0.20, 1.95]
Papadopoulos 2013	2	25	2	25	2.1%	1.00 [0.13, 7.72]
Paugh 2015	398	1362	1241	5045	82.4%	1.27 [1.11, 1.45]
Raman 2003	6	61	10	57	7.2%	0.51 [0.17, 1.52]
Zhang 2009	0	60	1	60	0.9%	0.33 [0.01, 8.21]
Total (95% CI)		**1822**		**5506**	**100.0%**	**1.10 [0.81, 1.49]**
Total events	411		1263			

Heterogeneity: Tau² = 0.02; Chi² = 5.37, df = 5 (P = 0.37); I² = 7%
Test for overall effect: Z = 0.63 (P = 0.53)

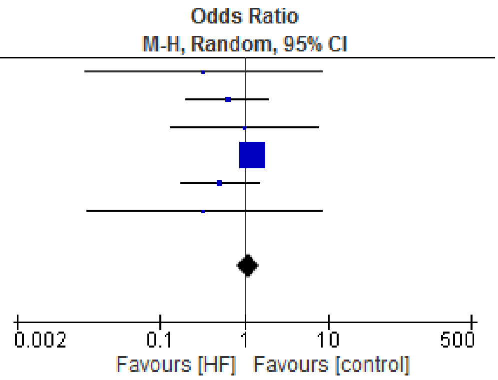

Figure 15. The results of meta-analysis on the association of Ultrafiltration and the acute renal failure

Study or Subgroup	HF Events	HF Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
de Baar 2013	1	29	2	31	14.9%	0.52 [0.04, 6.04]
Paugh 2015	35	1362	86	5045	44.2%	1.52 [1.02, 2.26]
Soliman 2016	17	138	38	145	40.9%	0.40 [0.21, 0.74]
Total (95% CI)		**1529**		**5221**	**100.0%**	**0.75 [0.24, 2.36]**
Total events	53		126			

Heterogeneity: Tau² = 0.74; Chi² = 12.99, df = 2 (P = 0.002); I² = 85%
Test for overall effect: Z = 0.50 (P = 0.62)

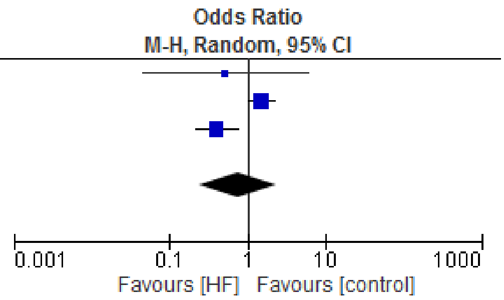

Figure 16. The results of meta-analysis on the association of Ultrafiltration and the IABP

Study or Subgroup	HF Events	HF Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
Babka 1997	0	30	2	30	1.8%	0.19 [0.01, 4.06]
Boodhwani 2009	3	29	2	36	5.0%	1.96 [0.31, 12.61]
Coşkun 2013	1	26	3	20	3.2%	0.23 [0.02, 2.37]
Naveed 2015	1	40	3	40	3.3%	0.32 [0.03, 3.18]
Oliver 2004	0	64	0	63		Not estimable
Papadopoulos 2013	4	25	5	25	8.3%	0.76 [0.18, 3.25]
Paugh 2015	23	1362	76	5045	78.5%	1.12 [0.70, 1.80]
Total (95% CI)		**1576**		**5259**	**100.0%**	**0.99 [0.65, 1.50]**
Total events	32		91			

Heterogeneity: Tau² = 0.00; Chi² = 4.53, df = 5 (P = 0.48); I² = 0%
Test for overall effect: Z = 0.06 (P = 0.95)

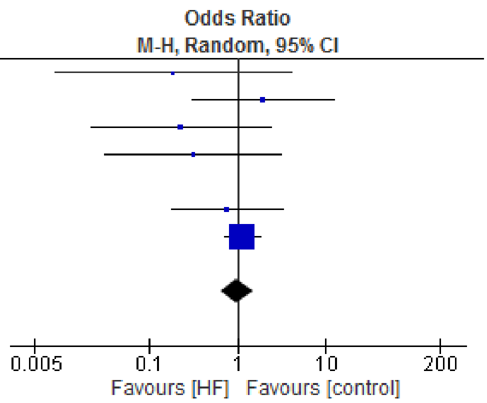

Figure 17. The results of meta-analysis on the association of Ultrafiltration and the reoperation

in patients with chronic kidney disease and cardiovascular disease as demonstrated in a study which examined increased UF rates in patients with ESRD and cardiovascular disease [28].

The length of stay in the ICU was also significantly decreased (mean difference -0.16 days) in the UF groups compared to the control groups. However, this statistical significance does not pertain a clinical significance as the duration of difference was marginal. Total time on ventilator, hospital length of stay, myocardial infarction, surgical site infections, arrhythmia, stroke, low cardiac output and the need for intra-aortic balloon pump, and reoperation were equivalent between the two groups.

Some limitations have surfaced while doing our review. We employed a broad search strategy but the possibility that important clinical trials were missed remains. Our goal was to report all clinical outcomes reported in different studies, which reflected a heterogeneity in the endpoints of these studies.

Conclusion

Based on the results from this meta-analysis, the use of UF during or after CBP decreases bleeding and transfusion requirements. No clear impact on mortality was seen and no discernable risk of acute kidney injury. We deduced that UF appears to be useful in adult cardiac surgery given the reductions in bleeding and blood product needs. It should be noted, however, that UF in patients with initially reduced kidney function should be used with caution. There are still gaps in evidence and larger randomized clinical trials should be performed.

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