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One-stage bilateral unicompartmental knee arthroplasty is a suitable option vs. the two-stage approach: a meta-analysis

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- To compare one-stage vs. two-stage bilateral unicondylar knee arthroplasty (UKA) in terms of complications, mortality, reinterventions, transfusion rate, days to discharge, and outcomes for the treatment of bilateral monocompartmental knee osteoarthritis.
- A systematic review was performed in the PubMed, Web of Science, and Cochrane databases up to February 2021. Randomized controlled trials, case-control studies, and case series describing the use of bilateral UKA were retrieved. A meta-analysis was performed on complications, mortality, reinterventions, transfusion rate, and days to discharge comparing one-stage vs. two-stage replacement, and outcomes were also reported. Assessment of risk of bias and quality of evidence was performed with the Newcastle-Ottawa Scale.
- Fifteen articles were included on 1451 patients who underwent bilateral UKA (44.9% men, 55.1% women, mean age 66 years). The systematic review documented, for bilateral one-stage UKA: 2.6% major and 5.4% minor complication rates, 0.5% mortality, 1.9% reintervention, 4.1% transfusion rates, and 4.5 mean days to discharge. No studies reported functional differences. The meta-analysis did not find differences for major complications, minor complications, mortality, reintervention, transfusion rates, or days to discharge versus two-stage bilateral procedures. The operative time was 112.3 vs. 125.4 minutes for one-stage and two-stage surgeries, respectively. The overall quality of the retrieved studies was high.
- Bilateral single-stage UKA is a safe procedure, with a few complications, and overall positive clinical results. No differences were found in terms of complications, mortality, reinterventions, transfusion rate, and days to discharge in comparison with the two-stage approach.

Keywords: bilateral UKA; knee replacement; one-stage; single-stage; two-stage; unicompartmental arthroplasty

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Introduction

The surgical treatment of knee osteoarthritis (OA) has been constantly growing for more than two decades, with more than 10 billion dollars spent every year on knee replacements in the US alone.¹ Traditionally, total knee arthroplasty (TKA) has been the treatment of choice even in young patients with moderate OA,^{2,3} although in the last years more and more attention has been paid to less invasive methods for patients with unicondylar OA.⁴ In this light, unicondylar knee arthroplasty (UKA) has become the treatment of choice for isolated medial or lateral femorotibial OA,^{5,6} both for patients under 60 years of age with an active style of life and for older patients.⁷⁻⁹ The advantages of UKA comprehend more controllable pain, lower complication rates along with good long-term survivorship and kinematics.^{10,11}

A great effort has been made to introduce and improve the minimally invasive approach for UKA surgery, allowing recovery to be shortened and the hospitalization time to be reduced and, therefore, reducing costs.¹²⁻¹⁴ To further reduce complications, inconveniences and costs, an increasing number of surgeons started implanting bilateral UKAs at the same time in patients with bilateral unicompartmental OA. However, there is an ongoing debate between proponents of a single-stage surgery and advocates of the two-stage approach. The first underlines shorter operative and total anaesthesia times, lower costs and similar clinical outcomes and satisfaction,¹⁵ while the second emphasizes the risk for higher complication rates and longer rehabilitation time.^{16,17}

The aim of this systematic review and meta-analysis was to understand the potential and the limitations of one-stage UKA for the treatment of bilateral unicompartmental OA, by documenting complications, mortality, reinterventions, days to discharge, and overall outcomes also by comparing one-stage vs. two-stage bilateral UKA.

Materials and methods

Literature search and data extraction

A review protocol was developed based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (www.prisma-statement.org), and it was registered on the International Prospective Register of Systematic Reviews (PROSPERO) (https://www.crd.york. ac.uk/prospero). An institutional review board endorsement was not obtained because all data were extracted from previously published studies. No external funding was received for the initiation or completion of this study.

A comprehensive systematic search was performed in the bibliographic databases PubMed, Web of Science, and Wiley Cochrane Library from inception up to 1 February 2021. We used the following medical keywords for initial screening "(UKA OR monocondylar knee OR unicompartmental knee OR monolateral knee) AND (bilateral OR monolateral OR simultaneous arthroplasty OR stag*)". Randomized controlled trials (RCTs), non-randomized comparative studies, and case series describing the use of bilateral UKA were retrieved. Articles in languages other than English, preclinical and ex vivo studies, and review articles were excluded.

Two independent reviewers (PF, CMTDL) screened all titles and abstracts. After this first screening, the articles that met the inclusion criteria were screened for full-text eligibility and were excluded if they met one of the exclusion criteria (Fig. 1). In case of disagreement between the two reviewers, a third reviewer was consulted to reach a consensus (CC). An electronic table for data extraction was created prior to the study using Excel (Microsoft). The following data were extracted: title, first author, year of publication, journal, type of study, level of evidence, population characteristics, type of intervention, surgery time, discharge time, blood loss, follow-up, complications, reinterventions, mortality, and functional outcome.

Assessment of risk of bias and quality of evidence

All studies were evaluated according to the level of evidence (LOE), using previously published criteria.¹⁸ To establish potential bias in the selected studies from

our protocol research, two reviewers independently assessed the methodological quality of each study using the Newcastle–Ottawa Scale,¹⁹ following the recommendations of the Cochrane Observational Studies Methods Working Group.²⁰ This is a worldwide-validated instrument designed for both comparative and non-comparative surgical studies, based on a 'star scale system' on three criteria: the selection of the study groups, the comparability of the groups, and ascertainment of either exposure or outcome of interest. Assessment of risk of bias and quality of evidence was completed independently for all outcomes by two authors (PF, CMTDL) and a third author (CC) solved any possible discrepancy to reach consensus.

Statistical analysis

The statistical analysis and the forest plot were carried out using R Statistical Software (https://www.r-project. org/).²¹ Taking into consideration possible heterogeneity among studies, a statistical test for heterogeneity was first conducted with the Cochran Q statistic and I² metric and the presence of heterogeneity was considered significant with I^2 values $\ge 25\%$. When no heterogeneity was found with $I^2 < 25\%$, a fixed-effect model was used to estimate the pooled rates and 95% confidence intervals (CIs). Otherwise, a random-effect model was applied, and an I² metric was evaluated for the random effect to check the correction of heterogeneity. The influence of using a single or double stage on complication, reintervention, and mortality, transfusion rates, and days to discharge was assessed using a z test on the pooled rates with their corresponding 95% Cls. Subgroup analyses for complications between single and double-stage techniques were made. A P value of 0.05 was used as the level of statistical significance.

Results

Study selection and analysis

After performing the exclusion process described above (Fig. 1), 15 studies were included for the final synthesis.^{15,22-35} All the retrieved articles were published between March 2009 and July 2020, three were conducted in Italy,^{26,31,33} three in the US,^{15,25,35} two in the UK,^{22,24} two in France,^{29,30} one in China,³² one in India,²⁷ one in Turkey,³⁴ one in Korea,²⁸ and one in Singapore.²³ Among the retrieved studies, six were case-controls comparing one-stage vs. two-stage UKA,^{15,22,23,30-32} five were case-controls comparing one-stage bilateral UKA vs. TKA,^{25,28} one RCT compared one-stage bilateral UKA vs. TKA,²⁷ and one was a case series about bilateral single-stage UKA (Table 1).²⁴

The systematic review was carried out on the bilateral one-stage UKA procedure of the 15 retrieved studies, for

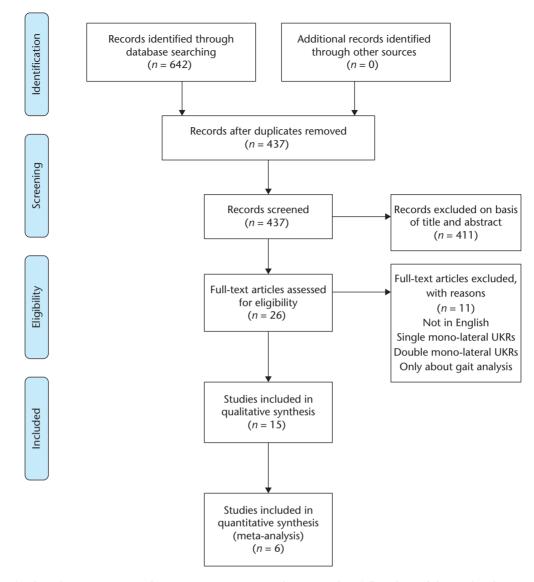


Fig. 1 PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart of the study selection process. *Note*. UKR, unicondylar knee replacement.

1451 patients (44.9% men, 55.1% women, mean age 65.6 years). Further details of the 15 selected studies have been reported in Table 1. The analysis of the overall literature documenting bilateral one-stage UKA results showed a major complication rate of 2.6% (pulmonary embolism was 1.0%, deep vein thrombosis was 0.8%, infection was 0.8%), a minor complication rate of 5.4%, a mortality rate of 0.5%, a reintervention rate of 1.9%, a transfusion rate of 4.1%, and an average of 4.5 days to discharge. None of the analysed studies reported functional differences between one-stage and two-stage bilateral UKA, nor between one-stage bilateral UKA and one-stage bilateral TKA, besides the 2011 case-control study by Berend et al¹⁵ reporting significantly better Lower Extremity Activity Score and Knee Society Function Score for the one-stage vs. the two-stage UKA group.

Meta-analysis: single-stage vs. two-stage bilateral UKA

Six case-control studies made a comparison between onestage vs. two-stage bilateral UKA and were used for the meta-analysis: they included 851 patients (35.7% men and 64.3% women), 452 in the first group, and 399 in the second. Mean age was 65.5 years (range 42–86 years) with no difference between the two groups; OA was the cause of knee replacement in all cases, but no details about OA grade were available for further evaluation of the possible correlation with the study findings. The mean follow-up period for all the studies was 27.4

Table 1. Summary of all studies' characteristics

Study	LoE	Journal	Techniques	Patie	nts	Age		Sex (F:N	1)	BMI		
				A	В	A	В	A	В	A	В	
Chan et al 2009 ²²	3	J Bone Joint Surg Br	One-stage vs. two- stage bilateral UKA	159	80	66.0 (42–85)	65.0 (48–86)	67:92	45:35	NA	NA	1
Berend et al 2011 ¹⁵	3	Clin Orthop Relat Res	One-stage vs. two- stage bilateral UKA	35	141	58.2 (55.4–62.1)	62.7 (61.2–64.2)	NA	NA	30.9 (29.4–32.4)	33.3 (32.1–34.5)	16.6
Chen et al 2013 ²³	3	J Bone Joint Surg [Br]	One-stage vs. two- stage bilateral UKA	124	47	62.9 (45–86)	61.6 (51.0–82.3)	91:33	36:11	27.3 (19.1–42.3)	26.8 (19.5–33.7)	24
Siedlecki et al 2018 ³⁰	3	Orthop Traumatol Surg Res	One-stage vs. two- stage bilateral UKA	44	26	69.2 (±9.4)	70.0 (±11.3)	24:20	19:7	9:7 26.8 (NA) 26.3		27.2
Biazzo et al 2019 ³¹	3	Musculoskelet Surg	One-stage vs. two- stage bilateral UKA	51	51	70.4 (68.0–72.8)	68.5 (65.4–71.7)	38:13	32:19	29.5 (28.1–30.9)	28.9 (27.5–30.5)	1
Feng et al 2019 ³²	3	BMC Musculoskelet Disord	One-stage vs. two- stage bilateral UKA	39	54	64.9 (±7.7)	64.2 (±6.4)	33:6	49:5	23.9 (±2.5)	23.5 (±2.6)	41.9
Romagnoli et al 2015 ²⁶	3	Int Orthop	Bilateral single- stage UKA vs. unilateral UKA	220	347	67.5 (66.3–68.6)	68.2 (67.3–69.2)	137:83	207:140	30.1 (29.4–30.9)	28.8 (28.2–29.3)	6
Clavé et al 2018 ²⁹	3	Orthop Traumatol Surg Res	Bilateral single- stage UKA vs. unilateral UKA	50	100	64.4 (50.0–86.7)	68.1 (56.0–86.7)	15:35	34:66	28.8 (22.1–38.9)	29.7 (21.9–47.6)	52.8
Yildiz et al 2019 ³⁴	3	Bezmialem Science	Bilateral single- stage UKA vs. unilateral UKA	44	137	66.1 (51–81)	64.9 (44–86)	34:10	110:27	33.0 (NA)	32.0 (NA)	27.7
Marullo et al 2019 ³³	3	Knee	Bilateral single- stage UKA vs. unilateral UKA	13	12	68.0 (±5.6)	69.8 (±4.4)	NA	NA	28.1 (±5.4)	28.2 (±1.9)	NA
Sakka et al 2020 ³⁵	3	Knee	Bilateral single- stage UKA vs. unilateral UKA	119	317	70.2 (47–94)	70.0 (39–89)	58:61	178:139	29.0 (20.3–43.0)	29.3 (18.4–47.0)	3
Winder et al 2014 ²⁵	3	Am J Orthop	Single-stage bilateral UKA vs. bilateral TKA	28	56	64.0 (±9.0)	64.0 (±9.0)	12:16	24:32	NA	NA	3
Kulshrestha et al 2017 ²⁷	2	J Arthroplasty	Single-stage bilateral UKA vs. bilateral TKA	36	36	59.7 (±8.7)	62.2 (±6.4)	30:6	26:10	28.3 (±3.4)	27.5 (±4.3)	24
Ahn et al 2017 ²⁸	3	Orthop Traumatol Surg Res	Single-stage bilateral UKA vs. unilateral TKA	52	52	65.1 (49–87)	65.6 (51–83)	4:48	4:48	28.1 (22.0–35.2)	28.3 (21.8–37.9)	6
Akhtar et al 2014 ²⁴	4	Knee	Bilateral single- stage UKAs	38	/	64 (43–80)	/	22:16	/	29.8 (17.0–48.2)	/	30

Note. LoE, level of evidence; F, female; M, male; BMI, body mass index.

months, with a range of 32-133 months. There was a statistically significant difference in body mass index (BMI) between the single-stage and the two-stage groups, with means of 27.6 and 25.4 respectively (p < 0.01). American Society of Anesthesiologists (ASA) classes of the included patients were not comparable since no study provided them. For the operatory time, the pooled mean was 112.3 min in the one-stage group vs. 125.4 min in the two-stage group, but a meta-analysis was not performed since most of the studies provided incomplete data. Similarly, while all studies documented a significant clinical improvement with no differences between the two approaches, a meta-analysis of the functional outcomes was not possible due to the heterogeneity of the data.

A meta-analysis was performed instead on other significant treatment outcomes:³⁶⁻³⁹ major and minor complications, mortality, reinterventions, transfusion rate, and days to discharge (Fig. 2). No statistically significant difference was found in any of these aspects between one-stage and two-stage groups, as documented in Fig. 2. In detail, the major complication rate was 4.40% and 2.30% (n.s.) and the minor complication rate was 4.4% vs. 9.3% in the one-stage and two-stage groups, respectively (n.s.) (Fig. 3). The p-value was not assessable (n.a.) for mortality and reinterventions, since mortality was 0.2% in the one-stage group and 0% in the two-stage group, while reintervention was 0% in the first group and 0.5% in the second. The transfusion rate was 1.5% in the one-stage group and 0.8% in the two-stage group (n.s.) (Fig. 3), and the mean time to discharge was 4.8 days in the one-stage group vs. 5.7 days in the two-stage group (n.s.) (Fig. 3). A more detailed analysis of the complications showed an infection rate of 1.5% in the first group and 1.8% in the second (n.s.), pulmonary embolism in 1.8% of patients who had a one-stage operation and 0% in the two-stage group (n.s.), and the deep vein thrombosis rate was 1.1% in the one-stage group and 0.5% in the two-stage group (n.s.).

Major Complication Rate

Study	Experin Events		Cont Events		Risk Ratio	RR	95%-CI	Weight (fixed)	Weight (random)
Chan, 2009	14	159	2	80	- <u> -</u>	3.52	[0.82; 15.12]	22.2%	31.8%
Berend, 2011	0	35	0	141				0.0%	0.0%
Chen, 2013	3	124	5	47	li	0.23	[0.06; 0.91]	60.4%	33.0%
Siedlecki, 2018	2	44	1	26		1.18	[0.11; 12.40]	10.5%	19.4%
Biazzo, 2019	0	51	0	51	li li			0.0%	0.0%
Feng, 2019	1	39	1	54		1.38	[0.09; 21.47]	7.0%	15.8%
Fixed effect model		452		399		1.14	[0.53; 2.42]	100.0%	
Random effects mod Heterogeneity: $/^2 = 59$) 8342	n = 0.06			1.00	[0.13; 7.77]		100.0%
fictorogeneity. / = J.	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	,J+Z,	ρ = 0.00		0.1 0.5 1 2 10				

Minor Complication Rate

	Experim	ental	Cont	trol				Weight	Weight
Study	Events	Total	Events	Total	Risk Ratio	RR	95%-CI	(fixed)	(random)
Chan, 2009	3	159	3	80		0.50	[0.10; 2.44]	15.0%	14.5%
Berend, 2011	4	35	29	141		0.56	[0.21; 1.48]	43.3%	30.6%
Chen, 2013	2	124	0	47		1.91	[0.09; 39.01]	2.7%	4.5%
Siedlecki, 2018	4	44	4	26		0.59	[0.16; 2.16]	18.9%	20.0%
Biazzo, 2019	4	51	2	51		2.00	[0.38; 10.44]	7.5%	13.4%
Feng, 2019	3	39	4	54		1.04	[0.25; 4.38]	12.6%	17.0%
Fixed effect model		452		399		0.76	[0.43; 1.34]	100.0%	
Random effects mo	del					0.77	[0.44; 1.37]		100.0%
Heterogeneity: $/^{2} = 0$	$0\%, \tau^2 = 0.$	1137, r	0 = 0.75						
5 5					0.1 0.5 1 2 10				

Mortality Rate

	Experi	mental	Cont	trol				Weight	Weight
Study	Events	Total	Events	Total	Risk Ratio	RR	95%-CI	(fixed)	(random)
Chan, 2009	1	159	0	80		1.51	[0.06; 36.75]	100.0%	100.0%
Berend, 2011	0	35	0	141				0.0%	0.0%
Chen, 2013	0	124	0	47				0.0%	0.0%
Siedlecki, 2018	0	44	0	26				0.0%	0.0%
Biazzo, 2019	0	51	0	51				0.0%	0.0%
Feng, 2019	0	39	0	54				0.0%	0.0%
Fixed effect model Random effects mo Heterogeneity: / ² = 1		452 NA, <i>p</i> =	= NA	399	0.1 0.5 1 2 10	1.52 1.51	[0.06; 36.87] [0.06; 36.75]	100.0% 	 100.0%

Reintervention Rate

	Experin	nental	Cont	trol				Weight	Weight
Study	Events	Total	Events	Total	Risk Ratio	RR	95%-CI	(fixed)	(random)
Chan, 2009	0	159	0	80				0.0%	0.0%
Berend, 2011	0	35	2	141		0.80	[0.04; 16.24]	100.0%	100.0%
Chen, 2013	0	124	0	47				0.0%	0.0%
Siedlecki, 2018	-	44	-	26				0.0%	0.0%
Biazzo, 2019	0	51	0	51				0.0%	0.0%
Feng, 2019	0	39	0	54	i i			0.0%	0.0%
Fixed effect model Random effects mo		452	NIA	399		0.79 0.80	[0.04; 16.07] [0.04; 16.24]	100.0% 	 100.0%
Heterogeneity: $/^2 = 1$	NA%, τ² =	NA, p =	= NA		0.1 0.5 1 2 10				

(continued)

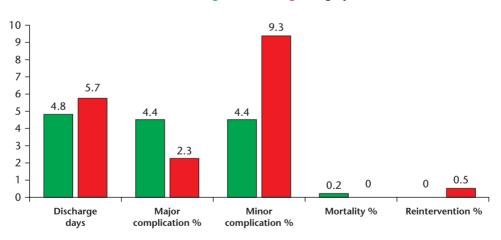
Transfusion Rate

Study	Experir Events		Cont Events			Ri	sk Rati	0		RR	95%-CI	Weight (fixed)	Weight (random)
Chan, 2009	0	159	0	80								0.0%	0.0%
Berend, 2011	0	35	0	141								0.0%	0.0%
Chen, 2013	1	124	0	47						1.14	[0.05; 27.61]	13.3%	21.7%
Siedlecki, 2018	1	44	3	26		1				0.20	[0.02; 1.80]	69.6%	32.2%
Biazzo, 2019	4	51	0	51						9.00	[0.50; 162.93]	9.2%	24.3%
Feng, 2019	1	39	0	54		_		*		4.14	[0.17; 98.97]	7.8%	21.8%
Fixed effect model		452		399				>		1.44	[0.51; 4.09]	100.0%	
Random effects mo Heterogeneity: $/^2 = 4$		1.5409	n = 0.17		[1.42	[0.09; 23.66]		100.0%
			, p 0.17		0.01	0.1	1	10	100				

Days of Discharge

	Experin		Cont					Weight	Weight
Study	Events	lotal	Events	lotal	Risk Ratio	RR	95%-CI	(fixed)	(random)
Chan, 2009	5.0	159	6.0	80		0.42	[0.13; 1.33]	18.0%	20.2%
Berend, 2011	1.7	35	2.5	141		2.74	[0.40; 18.55]	2.2%	12.0%
Chen, 2013	5.0	124	8.0	47		0.24	[0.08; 0.69]	26.2%	21.5%
Siedlecki, 2018	6.7	44	13.9	26		0.28	[0.13; 0.62]	39.4%	25.7%
Feng, 2019	4.2	39	7.5	54		0.78	[0.25; 2.38]	14.2%	20.7%
Fixed effect model		401		348		0.42	[0.27; 0.67]	100.0%	
Random effects me	odel					0.48	[0.16; 1.39]		100.0%
Heterogeneity: /2 =	42%, τ ² =	0.5318,	<i>p</i> = 0.14						
					0.1 0.5 1 2 10				

Fig. 2 Forest plot of the meta-analyses; from the top to bottom: Major Complication Rate, Minor Complication Rate, Mortality Rate, Reintervention Rate, Transfusion Rate, Days of Discharge.



One-stage vs Two-stage Surgery

Study quality and risk of bias

Among the retrieved studies, one was a LOE 2 RCT,²⁷ 13 were LOE 3 case-control studies,^{15,22,23,25,26,28-35} and one was a LOE 4 case series.²⁴ The quality of the studies selected was judged overall to be high, with none of the included papers deemed to have a high risk of bias (Table 2). According to the Newcastle-Ottawa Scale,¹⁹ two studies have awarded a total of 7 stars,^{31,35} three studies 8 stars,^{26,30,34} and the other 10 the maximum possible score of 9 stars.^{15,22-25,27-29,32,33}

Fig. 3 Main outcomes of the studies on 'one-stage vs. two-stage bilateral UKA'.

Study	Туре	Selection	Comparability	Exposure/ Outcome	Total number of star	
Chan et al 2009 ²²	R	****	* *	***	9	
Berend et al 2011 ¹⁵	R	****	**	***	9	
Chen et al 2013 ²³	Р	****	**	***	9	
Akhtar et al 2014 ²⁴	С	****	* *	***	9	
Winder et al 2014 ²⁵	R	****	**	***	9	
Romagnoli et al 2015 ²⁶	R	****	**	$\diamond \diamond \diamond$	8	
Kulshrestha et al 2017 ²⁷	RCT	****	**	***	9	
Ahn et al 2017 ²⁸	R	****	**	***	9	
Clavé et al 2018 ²⁹	Р	****	**	***	9	
Siedlecki et al 2018 ³⁰	R	****	**	$\diamond \diamond \diamond$	8	
Biazzo et al 2019 ³¹	R	****	**	$\diamond\diamond\diamond$	7	
Feng et al 2019 ³²	R	****	**	***	9	
Marullo et al 2019 ³³	Р	****	**	***	9	
Yildiz et al 2019 ³⁴	R	****	•	**	8	
Sakka et al 2020 ³⁵	R	****	$\diamond \diamond$	***	7	

Table 2. Qualit	y of the studies included, according to the Newcastle–Ottawa Scale
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Note. RCT, randomized controlled trial; P, prospective comparative study; R, retrospective comparative study; C, case series (retrospective).

Discussion

The most important finding of this systematic review and meta-analysis is that bilateral single-stage UKA is a safe procedure, with the one-stage approach offering good clinical results without incurring higher risks than the two-stage bilateral UKA. These findings are of clinical relevance, due to the high socio-economic costs of patients affected by OA and in particular those undergoing prosthetic resurfacing.⁴⁰ The single-stage approach avoids one extra surgery, thus reducing total hospitalization length, operatory time and, consequently, total costs of the procedure. Thus, while these aspects must be further evaluated in the future with specific RCT studies to better quantify their real impact on healthcare systems and society, this meta-analysis dissipates doubts of possible negative impacts on the patient. The pooled literature showed an overall low number of complications and no statistically significant differences in the results versus the twostage approach. The meta-analysis investigated major as well as minor complications. One-stage surgery had slightly more major complications (infection, pulmonary embolism, deep vein thrombosis) as compared to doublestage surgery (4.4% vs. 2.3%), but these values were not statistically significant. Moreover, it is important to notice that these potentially life-threatening complications did not imply more deaths or reinterventions in one-stage surgeries. On the contrary, the minor complication rate was slightly higher in two-stage surgeries (9.3% vs. 4.4%), although also in this case without any statistical significance. Considering that these data were retrieved from a pool of more than 850 patients, this allows us to suggest the safety and feasibility of single-stage bilateral UKA, with the meta-analysis results supporting what other authors have previously suggested in smaller series.^{15,23,30-32} To further strengthen these findings, pooled complications were investigated also including cohorts of patients not

included in comparative trials versus two-stage UKA, thus allowing us to draw evidence on complications from 15 studies on 1052 patients undergoing bilateral one-stage UKA. The major complication rate was 2.6% and the minor complication rate was 5.4%, confirming the overall low risks of complications.

Further analysis was performed to investigate complication rates in more detail: pulmonary embolism was 1.0%, deep vein thrombosis was 0.8%, and infection was 0.8%. Such a low incidence of pulmonary embolism and deep vein thrombosis is an important finding because when approaching inferior limb surgery there are always concerns regarding vascular thromboembolic events, especially when having a bilateral concomitant surgery limiting patient mobility in the post-surgery recovery phase. However, it must be underlined that UKA surgery has evolved over the years into a mini-invasive approach, and this could be the explanation for such a low incidence of such events. The post-operative infection rate was 0.2% and the reintervention rate was 1.9%, in line with bilateral two-stage UKA and with other literature findings on prosthetic resurfacing.^{41,42} Also with regard to the mortality rate of 0.5 %, only two of the five deaths among the 1052 patients operated with bilateral single-stage approach were actually linked to the UKA procedures according to what was reported by the authors.^{22,26}

Overall, these elements concur to support the onestage bilateral approach from the patient perspective. Moreover, other elements also favour it with regard to the patient-management healthcare perspective. In light of the increasing pressure toward cost reduction, an important aspect is the analysis of the days to discharge: the meta-analysis on one-stage vs. two-stage case-control studies^{15,22,23,30-32} provided solid evidence for this parameter because patients in both groups were treated at the same hospital, by the same staff and with the same protocol. The overall result retrieved was a mean of 4.8 days

for one-stage surgery and 5.3 days for two-stage surgery. Although the difference was not statistically significant, one-stage surgery demonstrated not to increase and actually to even slightly reduce the time of hospitalization. Moreover, the one-time hospitalization implies numerous advantages; on the one hand, patients solve two problems at once with all the consequent benefits such as one-time sick leave and follow-up visits halved; on the other hand, the hospital has to plan only one operating room, with all the positive logistic and economical consequences such as the need for only one surgical team organization and one instrument set. In this regard, when evaluating the retrieved studies about bilateral single-stage UKA, nine articles stated that bilateral UKAs were performed by the same team, 24-26, 28, 29, 32-35 while only three articles 22, 27, 30 declared that two teams were involved (all the remaining articles did not clarify this detail). In addition, the operatory time in the two procedures, quantified by pooling the literature data, shows an advantage of the one-stage approach, at an average of 112.3 min vs. the 125.4 min taken for the two-stage surgeries. This is another important element to be considered for the direct implications in anaesthesia-related risks and costs.⁴³ Due to the lack of data of the retrieved studies about the cost aspect, we did not perform a specific economic analysis on costs between single-stage and two-stage bilateral UKA. However, six of the retrieved studies^{23-25,30-32} took into account the economic aspect, all underlining a reduction of costs ranging from 12.5% to 43.7% in favour of the simultaneous operation. More specific studies should address this key aspect. This may imply significant healthcare and social impact considering the large and increasing number of OA patients requiring surgery.

Finally, higher blood loss could appear to be a possible downside of single-stage bilateral UKA, especially when addressing older patients with comorbidities. The meta-analysis showed a negligible difference, with 1.5 vs. 0.8% transfusion rates in one-and two-stage procedures. This value increases when considering all published data about bilateral one-stage UKA, reaching a value of 4.1%. While this remains an overall low percentage, blood loss should be further investigated, taking into account not only the transfusion rate but also the changes in haemoglobin values and their clinical consequences, identifying patients at more risk, and evaluating all the available strategies for reducing bleeding, such as tranexamic acid, which is safely and successfully used for knee surgery.⁴⁴⁻⁴⁶

The meta-analysis supported the feasibility of bilateral one-stage UKA both in terms of patient management and safety, but due to data heterogeneity, it could not address another key aspect when evaluating this approach: the functional outcome. Still, the literature presents concordant indications on this matter with all studies reporting satisfactory results. Among studies directly comparing functional results of one-stage vs. two-stage UKA, no differences in Knee Society Functional and Clinical Scores were reported by Feng et al at one-year followup, for either the right or left knee,³² and Chen et al²³ found no functional differences between one-stage and two-stage patients in Oxford Knee Score (OKS) and Knee Society Function Score at two-year follow-up. Moreover, the case-control study by Berend et al¹⁵ reported no difference in Knee Society Pain and Clinical Scores, and even significantly better Lower Extremity Activity Score and Knee Society Function Score for the one-stage versus the two-stage surgery, at 19.4 and 13.9 months of follow-up, respectively. Accordingly, the overall evidence on bilateral one-stage UKA supports good functional outcomes, not inferior to those of two-stage procedures, another crucial element to put into the equation when choosing the appropriate surgical protocol for a patient with bilateral mono-compartmental OA.

Finally, Kulshrestha et al²⁷ compared bilateral singlestage UKRs and bilateral single-stage TKA in the only RCT retrieved on this topic and found no difference between the two groups in terms of functional outcomes and patients satisfaction at two-year follow-up.27 Moreover, no complications, readmissions or reinterventions were observed for the UKA group, with shorter hospital stays. This RCT concluded that, contrarily to a common belief on the superiority of TKA, UKA and TKA provide similar functional outcomes, activity levels, and patient satisfaction for isolated medial compartment OA but, thanks to the decreased complications, rapid early rehabilitation, and ease of revision, UKA could be a more suitable option for patients with isolated medial compartment OA disease. Similar conclusions were also reached by a comparative non-randomized trial at a short-term follow-up, which stated that bilateral UKA has a low complication rate and has lower operative times and hospital lengths of stay when compared to an age, gender, and ASA score matched group of bilateral TKA patients.²⁵ While these findings are promising, they remain weakly supported by a limited number of studies, and further research efforts should support these results.

The limitations of this meta-analysis reflect the limits of the available studies. First of all, four of the retrieved studies had a follow-up < 6 months, making it impossible to see long-term complications in the analysed series of patients. Although not confirmed by the data in our possession, another possible limitation of non-randomized studies is the risk of bias introduced by the indication process for surgeons choosing to use the one-stage approach in patients with fewer comorbidities or better general health. While the overall quality of the retrieved studies was judged as high according to the Newcastle-Ottawa Scale,¹⁹ only one RCT²² was available, and this hampers the possibility of a meta-analysis with the highest evidence. Moreover, the small number of studies included reflects the paucity of scientific attention on this increasingly performed approach in clinical practice, especially when considering comparative investigations. The advantages of the minimally invasive UKA surgery could be further extended and, while high-level studies are still needed to better demonstrate and further improve the potential of this approach, this meta-analysis underlined the safety and successful results of addressing bilateral mono-compartmental OA with one-stage UKA.

Conclusions

This meta-analysis documented that bilateral singlestage UKA is a safe procedure, with few complications, and overall positive clinical results. No differences were found in terms of complications, mortality, reinterventions, transfusion rate, and days to discharge in comparison to the two-stage approach. Based on the available evidence, bilateral one-stage UKA is safe and effective, avoiding one surgery and related costs and impact to the patient and healthcare system, proving to be a suitable option for the treatment of bilateral mono-compartmental knee OA.

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