VALVE POSITIONS UPON WHICH CARDIAC SURGEONS OPERATE SHOULD BE TAKEN INTO CONSIDERATION

We read the article entitled "Mechanical versus bioprosthetic valves in chronic dialysis: a systematic review and meta-analysis" by Kim and colleagues,1 with great interest. The authors attempted to address limitations of previous meta-analyses by expanding the searching strategy and exhausting more databases without placing any language restriction. They concluded that the significant benefit of lower all-cause mortality with the use of mechanical prosthesis (MP) was at the expense of higher risks of bleeding and stroke. We appreciated the authors' efforts and contribution, and concur with the authors that most studies were subject to high risk of unmeasured confounding bias owing to unreported demographics, which lowers the

quality of evidence considerably. However, we believe that the prosthetic position upon which cardiac surgeons operate is a significant contributor to not only conceptual, but also statistical heterogeneity. Besides, compared with relative risk (RR) that Kim and colleagues selected for the analysis of all-cause mortality, hazard ratio (HR) is supposed to be a more appropriate statistic, as it incorporates time into the consideration.

Thus, we followed Kim and colleagues' inclusion criteria and reconducted the meta-analysis with the introduction of a subgroup analysis based on valve position. There are 8 studies²⁻⁹ providing comparative long-term survival outcome for aortic valve replacement (AVR) between MP and bioprosthesis (BP) in dialysis patients. We showed that dialysis patients using MP for AVR was associated with significantly lower longterm all-cause mortality than those using BP (HR 0.65, 95 % confidence interval [CI] 0.51-0.83, $I^2 = 0\%$) (Figure 1). On the other hand, the long-term overall survival was comparable between MP and BP (HR 0.91, 95 % CI 0.77–1.07, $I^2 = 0$ %) (Figure 1) in mixed cohorts of AVR and mitral valve replacement (MVR). Regarding the bleeding events, although the use of MP was associated with a considerably higher risk in studies including mixed cohorts of AVR and MVR (incidence rate ratio [IRR] 2.37, 95% CI 1.34–4.22, $I^2 =$ 41%), we found that there was no significant difference in bleeding events between MP and BP in patients undergoing AVR (IRR 1.18, 95% CI $0.28-4.85, I^2 = 0\%$) (Figure 1). One plausible explanation for similar bleeding risk between MP and BP in dialysis patients undergoing AVR may reside in the lower target of international normalized ratio (INR), usually less than 2.5, used in this population, as compared with the target of 3.0 used in MVR.28 In fact, it

	Long-term all-cause mortality							Bleeding events									
Study or subgroup	TE	SE	Weight	Hazard ratio IV, Random, 95% Cl	Hazard ratio IV, Random, 95% Cl		Study or subgroup E	Ex vents	perim Time	ental Events	Contr Time	ol Weight	Incidence rate MH, Random, 9	ratio 5% CI	Incidence Ra MH, Random,	te Ratio 95% CI	
Nakatsu ⁶	-0.45	0.2700	5.3%	0.64 (0.38-1.09)			AVR										
Okada ⁷	-0.89	0.3750	3.3%	0.41 (0.20-0.86) -	÷		Nakatsu ⁶	42	420	68	808	15.6%	1.19 (0.81-	1.75)			
Fukui ⁴	-0.41	0.4313	2.6%	0.67 (0.29-1.55)			Boning ²	0	61	0	23	15%	0.38 (0.01-19	a 00) —			
Boning ²	-0.45	0.6316	1.3%	0.64 (0.19-2.21) -			Total (95% C	n Ö	01	0	20	170%	1 18 (0 25-	1.95)		-	
Thourani ⁹	-0.20	0.3062	4.5%	0.82 (0.45-1.49)	-		10tal (35% C	", 				17.070	1.10 (0.25-	+.03)			
Tanaka ⁸	-1.02		Heterogeneity: $Iau^2 = Cht^2 = 0.33$, $dt = 1$ ($p = 0.57$), $t^2 = 0\%$														
Filsoufi ³	-0.33	0.2762	5.2%	0.72 (0.42-1.24)													
Hori⁵	-0.27	0.3199	4.2%	0.76 (0.41-1.42)			MVR and/or	AVR									
Total (95% (CI)		28.1%	0.65 (0.51–0.83)	-		Boeken ²³	7	132	7	180	9.7%	1.36 (0.48–3	3.89)		_	
Heterogeneity: Tau ² = Chi ² = 3.67, df = 7 (p = 0.82), l ² = 0%						Brinkman ²⁰	13	146	1	52	4.4%	4.63 (0.61–3	5.39)		-		
							Chan ¹⁸	1	41	0	57	2.1%	6.37 (0.26-15	6.27)			
MVR and/or	r AVR		700		<u>:</u>		D'Alessandro	¹⁵ 1	92	2	145	3.4%	0.79 (0.07-	3.69)			
Ikeno ¹⁰	-0.20	0.1938	7.9%	0.82 (0.56-1.20)			Earboo ²⁴	2/	219	9	199	12.2%	2 / 2 / 1 13	5 21)	14		
Chan''	-0.78	0.3519	3.6%	0.46 (0.23-0.92)			Forbes	27	210	0	741	6 E 0/	2.42 (1.10)	2.21/			
Manghelli ¹²	-0.24	0.1468	0.1%	0.79 (0.59-1.05)			Ikeno	2	320	9	/41	0.5%	0.51 (0.11–.	2.38)	-		
VVIIIIams ¹⁰	0.02	0.2358	0.3%	1.02 (0.64-1.62)			Kaplon ²²	5	94	3	138	7.1%	2.45 (0.58–10).24)		-	
Nakatsu ¹	-0.99	0.4959	Z.1% / 10/	0.37 (0.14-0.98)			Kato ²⁵	4	85	0	22	2.5%	2.33 (0.13–43	3.27)			
Zhibing ¹⁶	_0.22	1.0602	4.170	1.24 (0.00-2.34)			Lucke ²⁶	8	27	0	24	2.6%	15.11 (0.87-26	1.80)			
Thourani ⁹	0.33	0.2002	73%	1.37 (0.91_2.06)			Manghelli ¹²	10	105	6	436	10.0%	6.92 (2.52-1	9.04)		_	
I Imezu ¹⁷	0.64	0.5034	2.0%	1.89 (0.91_2.06)		_	Takota ²⁷	13	78	11	53	11.9%	0.80 (0.36-	1 79)			
Chan ¹⁸	-0.74	0.3421	3.8%	0.48 (0.24-0.93)			Taketa Taketa	7	30	1	59	1 2%	13 77 (1 69-11	1 90)		_	
Toole ¹⁹	0.46	0.4240	2.7%	1.59 (0.69-3.65)			100ie	,	50			4.2 /0	13.77 (1.05=11	1.03/	1		
Brinkman ²⁰	0.02	0.3742	3.3%	1.02 (0.49-2.12)			Umezu ^{1/}	5	151	1	90	4.1%	2.98 (0.35-2	5.51)		+	
Herzog ²¹	-0.02	0.0385	15.5%	0.98 (0.91-1.06)			Zhibing ¹⁶	2	129	0	141	2.3%	5.47 (0.26–11	3.83			
Kaplon ²²	-0.29	0.4025	2.9%	0.75 (0.34-1.65)			Total (95% C	I)				83.0%	2.37 (1.34–4	4.22)			
Total (95% (CI)			0.91 (0.77-1.07)	-		Heterogeneity: Ta	$au^2 = 0.$	04269, 0	Chi ² = 2	22.01, df	= 13 (p =	0.06), $I^2 = 41\%$				
Heterogeneity:	Tau ² = 0.02	79, Chi ² = 2	22.27, df =	13 (p = 0.05), l ² = 42%													
Tetel (0E%) (21)		00.00/	0.02 (0.71.0.00)			Total (95% C	I)				100%	2.06 (1.24-3.43	;)	-	•	
							Heterogeneity: Tau ² = 0.3723. Chi ² = 26.90. df = 15 (p = 0.03). l ² = 44%										
Heterogeneity: Iau ² = 0.0359, Ch ² = 35.30, at = 21 (p = 0.03), i ² = 41% Turt for a thread of the second seco							Test for subgroup differences: $Ch^2 = 5.95 \text{ df} = 1 (\rho = 0.01)$ 0.01 0.1 1 10								10 100		
Iest for subgrou	ip amerence	is: cniř = 5.	10, ai = 1 (j	Favours		Favours								Favours	S cal	Favou	
				mechanica	I	biological								valve	cai	valv	

Fig. 1. Forest plot of comparative long-term all-cause mortality and bleeding events between mechanical and bioprosthetic prosthesis. Meta-analyses were carried out using random-effects model with restricted maximum likelihood as an estimator for betweenstudy variance.

has been shown in previous meta-analysis that MP conferred a significantly greater bleeding risk than BP when INR was above 2.5, while bleeding events were comparable when INR was below 2.5.²⁹ Of note, the valve position appeared to be a significant contributor to heterogeneity as both subgroup analyses revealed significant quantitative interaction between different valve positions (p = 0.02 for long-term, all-cause mortality and p = 0.01 for bleeding events) (Figure 1). In summary, when taking the valve position into consideration, our subgroup analysis revealed that MP may be a feasible choice in dialysis patients undergoing AVR given significant lower long-term all-cause mortality with comparable bleeding risk as compared with BP.

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