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Therapeutic Applications of Drug-Coated Balloons in Symptomatic Intracranial Arterial Stenosis: A Systematic Review and Quantitative Meta-Analysis

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Introduction

- Intracranial atherosclerotic stenosis (ICAS) is a major cause of stroke[1-3], with interventional procedures often complicated by adverse events, such as procedural complications, in-stent restenosis, and ischemic events, which pose significant challenges to effective treatment[4-6].
- While drug-coated balloons (DCBs) have demonstrated efficacy in reducing restenosis in coronary artery disease, current evidence regarding their application in ICAS is limited to small-scale studies, and their safety and efficacy in this context remain to be conclusively established[7].
- Therefore, We conducted a systematic review and meta-analysis to evaluate the safety and efficacy of DCBs compared with other endovascular treatments for symptomatic ICAS, aiming to provide evidence to support clinical decision-making.

Methods

Search strategy

A comprehensive literature search was performed in PubMed, Embase, CNKI, and Wanfang from inception to October 16, 2023. A combination of MeSH terms and free-text keywords was used to ensure broad coverage, including 'intracranial', 'cerebral', 'arteriosclerosis', 'artery', 'steno*', 'occlus*', 'drug coat*', and 'drug elut*'.

Eligibility criteria

Studies were included if they met the following criteria:

- Patients were diagnosed with symptomatic ICAS, confirmed by clinical presentation and DSA.
- DCBs were used as the primary intervention for symptomatic ICAS.
- One or more of the following outcome measures were reported: restenosis cases, perioperative adverse events, technical success rates, or follow-up adverse events.

Quality assessment

Two reviewers independently assessed the reporting quality of the included studies using the Methodological Index for Non-Randomized Studies (MINORS) scale, which includes 8 items for non-controlled studies (total score=16) and 12 items for controlled studies (total score=24).

Statistical analysis

- Meta-analyses were conducted in R, using pooled ORs with 95% CIs.
- Heterogeneity was assessed with I^2 statistic; fixed or random effects models were selected accordingly.
- Freeman-Tukey transformation was applied to estimate the pooled rates for restenosis and safety outcomes, suitable for studies with zero events.
- Meta-regression was used to explore potential sources of heterogeneity.
- Egger's test was used to detect publication bias in single-arm studies.

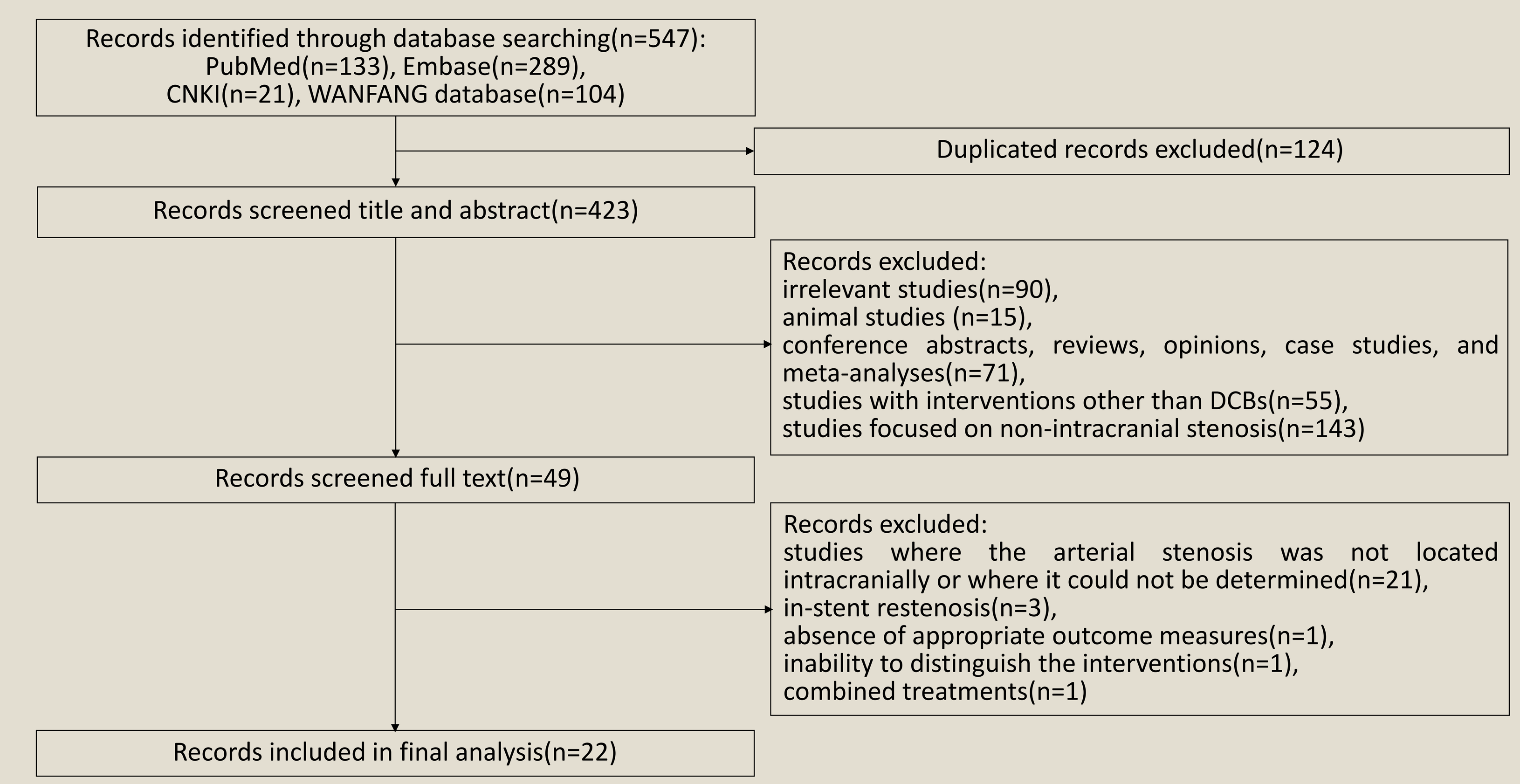

Fig. 1. PRISMA flow chart for study selection.

Results

- Overall, 22 studies were included in this review (Figure 1). The basic characteristics of the 16 observational single-arm studies and six controlled studies are presented in Table 1 and 2.

Rate of restenosis

- 16 single-arm studies reported restenosis rates, with pooled analyses showing rates of 7.81% per lesion (11 studies, 604 lesions) and 7.34% per patient (14 studies, 508 patients).
- Among controlled studies, DCBs significantly reduced restenosis risk compared to conventional balloons (OR=0.24, P<0.05) and stents (OR=0.20, P<0.05).

Perioperative safety

- Among 16 single-arm studies, the pooled periprocedural adverse event rate was 14.43%, and stroke or mortality was 5.75%.
- Five controlled studies showed a non-significant trend favoring DCBs over conventional balloons (OR=0.55) and stents (OR=0.56).

Follow-up safety

- Among 16 single-arm studies, the pooled incidence of follow-up adverse events was 2.03%, and 1.26% for stroke or TIA.

Table 1. Basic characteristics of the included controlled studies.

First author, Publication year	Country	Disease	Time horizon	Patients	Lesions	Males	Age/y	Intervention	Follow-up/ m	MINORS
Yang Y, 2023	China	sICAD	2017.3-2022.3	52	NR	25	48.3±10.6	SeQuent DCB	12	16
				52	NR	24	47.4±10.1	Stent (Enterprise)	12	
Tang Y., 2023	China	sICAS	2019.1-2021.8	49	49	38	54.0±9.6	SeQuent Please NEO	6*	16
				51	51	36	58.6±7.8	SacSpeed Balloon	6*	
Wang J., 2021	China	sICAD	2017.1-2021.6	16	16	9	62.7*(58.8-69.5)	SeQuent Please NEO	9.5(6.0-12.0) *	15
				13	16	8	61.8*(57.0-67.0)	Balloon (Tazuna, Ryujin, Gateway, Sprinter)	7.6(2.8-11.0) *	
				6	8	5	69.8*(68.0-75.5)	Stent (Wingspan, Solitaire, Apollo)	13.5(5.8-17.8) *	
Zhang J., 2020	China	sICAD	2016.1-2019.1	42	42	30	57.6±10.8	SeQuent Please NEO	185±33 days	17
				73	73	51	59.1±7.9	Stent	185±33 days	
Zhang S., 2022	China	ICAD	2017.1-2022.1	45	19	11	64.0*(62.0-74.0)	SeQuent Please NEO	311.6±185.6 days	11
					22	13	61.0*(55.3-65.0)	Balloon (Tazuna, Ryujin, Gateway, Sprinter)	252.4±200.9 days	
					9	4	67.5*(65.3-70.0)	Stent (Wingspan, Solitaire, Apollo)	501.4±286.2 days	
Gruber P., 2018	Switzerland	sICAS	2017.1-2022.1	8	NR	5	68.5 (52-76)	Neuro Elutax SV DEB	9.5 (4.5–27) *	16
				11	NR	5	67 (59-73)	Wingspan/Gateway stent system	10 (6–58) *	

Table 2. Basic characteristics of the included single-arm studies.

First author, Publication year	Country	Disease	Time horizon	Patients	Lesions	Males	Age/y	Intervention	Follow-up (Clinical, Imaging)/m	Technical success	Remedial stent	MINORS
Yang X., 2023	China	sICAS	2021.5-2022.7	24	NR	17	64±6	SeQuent Please NEO	10*, 7*	100%	4	11
Yang X., 2021	China	sICAS	2018.9-2020.5	48	51	34	61.6±10.5	SeQuent Please	8*, 5.5*	98%	1	10
Yang X., 2020	China	sICAD	2018.9-2019.12	16	19	15	63.1±9.2	SeQuent DCB	6.3, 5.6	100%	0	8
He Y., 2023	China	sICAS	2018.1-2021.8	49	49	38	54±10	SeQuent Please	12*, 6*	91.8%	15	9
Han J., 2019	China	sICAS	2016.9-2017.9	30	31	24	57.4±8.3	SeQuent Please	9.8±2.6, 7.0±1.1	100%	2	10
Jiang S., 2023	China	sICAD	NR	70	72	50	55.5*(46.8-66)	SeQuent Please	6±1	NR	NR	12
Yang M., 2023	China	sICAD	2020.1-2021.2	29	29	22	49*(35-56)	SeQuent DCB	4.1*(3.3-6.7)	NR	0	13
Qiao H., 2022	China	sICAD	2015.9-2021.3	242	250	156	69.2±12.2	SeQuent Please	> 1, 9.9±4.1	100%	18	10
Wang A., 2021	China	sICAD	2015.10-2018.4	35	39	20	61.3±9	SeQuent Please	20.9±9.8, 10.7±3.9	97%	3	11
Hao Y., 2022	China	sICATO	2016.1-2020.10	30	NR	16	57.3±10.12	SeQuent Please	7.0±3.7, 8.0±3.7	100%	8	9
Zhang Y., 2021	China	sICAS	2018.1-2020.10	7	NR	7	28.4±3.9	SeQuent Please	15.4±6.9, 6.6±4.2	100%	2	6
Zhao W., 2023	China	sICAO	2015.1-2021.7	148	148	100	58.0±9.1	SeQuent Please	25.8±15.8, 4.9±2.4	100%	52	12
Gruber P., 2019	Switzerland	sICAD	2016.9-2018.1	10	10	10	73*(69-77)	SeQuent Please NEO	3*(2-3)	100%	0	10
Remonda L., 2021	Switzerland	sICAS	2014-2019	33	35	27	72*(66-77)	Neuro Elutax SV or SeQuent Please NEO	9*(3-22)	NR	NR	10
Wang L., 2023	China	sICAS	2020.6-2021.12	40	40	32	54.5±9.9	DCB	8.9±2.1	100%	13	6
Xu G., 2023	China	sICAS	2017.1-2021.12	80	80	55	59.4±11.2	Rapamycin-eluting balloon	8.7±2.0	100%	NR	8

*: median(quartile); NR: not report.

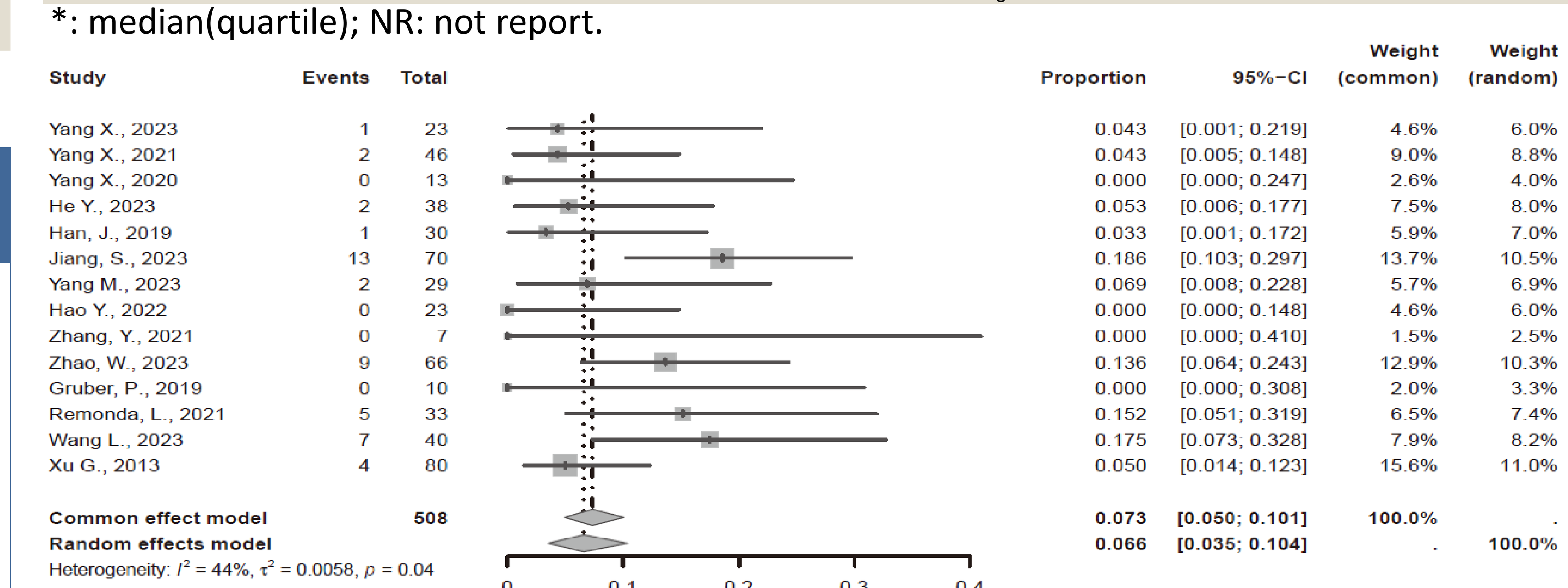

Fig. 2. Forest plot of restenosis rates in patients treated with DCBs (Patients unit).

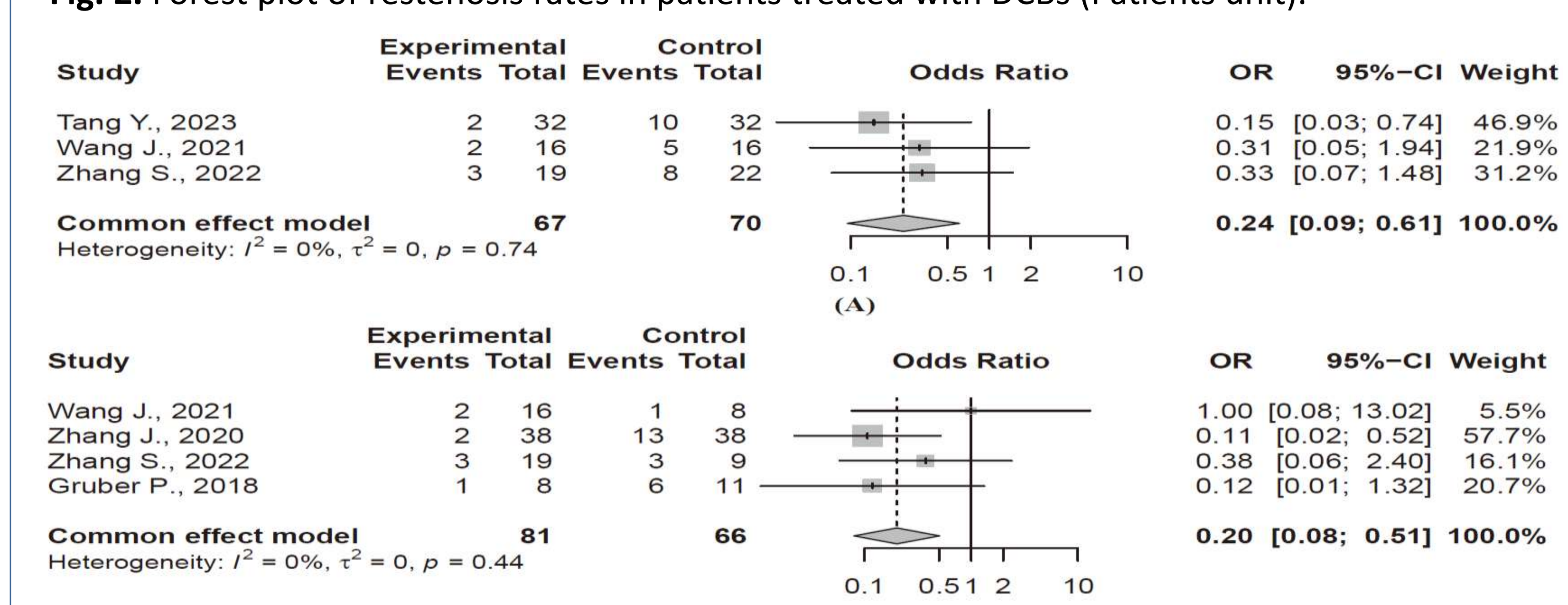

Fig. 3. Forest plot of restenosis rates in patients treated with DCBs. (A) Compared to balloons. (B) Compared to stents.

Conclusion

- This study showed that DCBs significantly reduced restenosis rates while maintaining a favorable safety profile in the treatment of ICAS.
- With perioperative stroke and mortality rates comparable with stent-based interventions and a low incidence of strokes and transient ischemic attacks (TIAs) during follow-up, these findings support the potential clinical integration of DCBs.
- Further prospective, large-scale studies with rigorous methodologies are needed to confirm long-term outcomes and optimize their use in intracranial applications.

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