



Hydrogel-coated versus bare platinum coils for intracranial aneurysms: a post-HYBRID updated meta-analysis of six randomized controlled trials

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PURPOSE

Randomized controlled trials (RCTs) comparing hydrogel-coated coils (HGCs) with bare platinum coils (BPCs) have yielded heterogeneous results, and the clinical relevance of longitudinal angiographic assessment remains uncertain. Following the publication of the HYBRID trial, which emphasized occlusion trajectory rather than static end points, a post-HYBRID updated meta-analysis is warranted to compare angiographic durability and safety outcomes between these coil types.

METHODS

A systematic literature search of MEDLINE, Web of Science, and Scopus was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. RCTs comparing HGCs with BPCs for the treatment of intracranial aneurysms were included.

RESULTS

Six RCTs comprising 2,486 patients and 2,513 treated intracranial aneurysms were included in the analysis. There was no statistically significant difference between HGCs and BPCs in immediate complete occlusion [risk ratio (RR): 0.87; 95% confidence interval (CI), 0.70–1.09; I^2 : 63.0%] or immediate adequate occlusion (RR: 0.96; 95% CI, 0.85–1.07; I^2 : 31.0%). Immediate residual aneurysm was significantly more frequent with HGCs than with BPCs (RR: 1.12; 95% CI, 1.01–1.24; I^2 : 0.0%; $P = 0.041$). At the last available angiographic follow-up, complete occlusion, adequate occlusion, and residual neck rates remained comparable between HGCs and BPCs. However, residual aneurysm at follow-up was significantly less frequent with HGCs than with BPCs (RR: 0.75; 95% CI, 0.68–0.83; I^2 : 0.0%; $P = 0.006$). HGCs were also associated with a significantly lower rate of major recurrence than BPCs (RR: 0.71; 95% CI, 0.54–0.94; $P = 0.024$). Safety and clinical outcomes were similar between treatment groups.

CONCLUSION

Despite comparable safety and clinical outcomes between HGCs and BPCs, HGCs demonstrated superior angiographic durability, as reflected by lower rates of residual aneurysm and major recurrence.

CLINICAL SIGNIFICANCE

HGCs may offer improved long-term aneurysm durability compared with BPCs by reducing residual aneurysm and major recurrence without compromising safety or clinical outcomes. These findings support consideration of HGCs when durable occlusion is a priority in endovascular treatment planning for intracranial aneurysms.

KEYWORDS

Intracranial aneurysm, hydrogel-coated coil, bare platinum coil

Aneurysm recurrence after endovascular coiling remains a clinically significant issue, with reported rates of approximately 10%–12%.^{1,2} This is thought to be driven by incomplete or unstable thrombus formation within the aneurysm sac, inadequate packing density, and insufficient neointimal formation at the aneurysm neck. To address these limitations, hydrogel-coated coils (HGCs) have been developed to increase volumetric aneurysm filling through polymer expansion upon contact with blood, thereby enhancing packing density and promoting more durable aneurysm healing.³ Preclinical studies have demonstrated improved neointimal coverage and more stable aneurysm occlusion with hydrogel-based technologies than with conventional bare platinum coils (BPCs), providing a strong biological rationale for their clinical application.⁴

Early-generation HGCs were evaluated in randomized controlled trials (RCTs) such as the HELPS trial,⁵ which demonstrated a reduction in major angiographic recurrence but failed to show a clear benefit in composite clinical outcomes, raising concerns regarding handling characteristics and delayed inflammatory complications. Subsequent device iterations led to the development of second-generation HGCs with improved flexibility and more controlled expansion profiles, prompting renewed investigation in randomized trials, including GREAT,⁶ HEAT,⁴ and PRET.⁷ However, these studies yielded heterogeneous results, with some trials reporting reduced recurrence or improved angiographic outcomes, whereas others failed to demonstrate superiority over BPCs, particularly in high-risk aneurysm populations.

Main points

- Superior long-term durability: Hydrogel-coated coils (HGCs) significantly reduced the rates of residual aneurysm and major recurrence at long-term follow-up compared with bare platinum coils (BPCs).
- Comparable safety profile: No significant differences in safety outcomes or clinical complications were observed between HGCs and BPCs, indicating comparable safety profiles, whereas angiographic differences did not translate into measurable clinical benefit.
- Initial vs. follow-up performance: Although HGCs were associated with higher immediate residual aneurysm rates than BPCs after the procedure, they demonstrated a superior occlusion trajectory, resulting in greater angiographic stability over time.

More recently, the HYBRID trial⁸ provided randomized evidence focusing specifically on recanalization as a primary end point and introduced a longitudinal assessment of angiographic evolution. Although the trial did not demonstrate a statistically significant difference in binary recanalization rates at 1 year, it revealed a significantly more favorable occlusion trajectory with HGCs than with BPCs, characterized by increased thrombosis and reduced progression to body filling. These findings underscore the importance of evaluating aneurysm occlusion as a dynamic process over time rather than relying solely on static dichotomous end points.

Two previous meta-analyses have attempted to synthesize randomized evidence comparing HGCs with BPCs. Earlier meta-analyses, which included only four RCTs,⁹ suggested lower mid-term recurrence and residual aneurysm rates with HGCs than with BPCs, particularly with second-generation devices, but were limited by small sample sizes, heterogeneous outcome definitions, and the absence of more recent randomized data. A subsequently published updated meta-analysis included only five RCTs¹⁰ and confirmed lower rates of major recurrence with HGCs than with BPCs; however, the authors acknowledged the limited number of included studies, the lack of long-term follow-up data, and prediction intervals that remained wide despite the available evidence.

Given the availability of new randomized evidence, the recognition that angiographic outcomes evolve over time, and the absence of any ongoing RCTs on this topic, a post-HYBRID updated meta-analysis using harmonized outcome definitions is warranted. At the time of writing, we were not aware of any ongoing RCTs addressing this topic. We therefore aimed to provide a comprehensive updated systematic review and meta-analysis comparing HGCs with BPCs for the endovascular treatment of intracranial aneurysms, with a particular focus on angiographic durability, recurrence patterns, and clinically meaningful outcomes.

Methods

This systematic review and meta-analysis were conducted in accordance with Cochrane Collaboration methodology and reported in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement.¹¹ Predefined eligibility criteria, outcome definitions, and analytical strategies followed the study protocol. This systematic review

and meta-analysis were not prospectively registered (e.g., in PROSPERO).

Eligibility criteria

Eligible studies were RCTs comparing HGCs with BPCs for the endovascular treatment of ruptured or unruptured intracranial aneurysms. Both first- and second-generation HGCs were considered eligible. Studies were required to report angiographic and/or clinical outcomes with a minimum follow-up duration sufficient to assess aneurysm occlusion status or recurrence. Studies were excluded if they were non-randomized, observational in design, case series, case reports, conference abstracts, technical notes without clinical outcome data, animal or *in vitro* studies, or if HGC outcomes could not be analyzed separately from BPC outcomes. Studies evaluating mixed or polymer-coated coils without hydrogel technology were also excluded.

Search strategy and study selection

A comprehensive literature search was performed across MEDLINE (PubMed), Web of Science, and Scopus from database inception through the final search date. The search strategy combined free-text terms and controlled vocabulary related to intracranial aneurysms, endovascular coiling, HGCs, and BPCs, including trial-specific terminology when applicable. The full search strategy is provided in Supplementary Table 1. Two reviewers independently screened titles and abstracts for relevance, followed by full-text assessment of potentially eligible studies. Disagreements were resolved through discussion and consensus. The study selection process is summarized in a PRISMA flow diagram.

Data extraction and quality assessment

Data extraction was independently performed by two reviewers using a standardized data collection form. Extracted data included study characteristics (study design, sample size, and follow-up duration), aneurysm characteristics (rupture status, size, neck width, and location), treatment details (coil type and use of adjunctive devices), and reported angiographic and clinical outcomes. When multiple follow-up time points were reported, the longest available follow-up was used for the primary analyses. If studies reported both per-protocol and intention-to-treat analyses, the intention-to-treat analysis was used.

The methodological quality and risk of bias of the included RCTs were independent-

ly assessed by two reviewers using the Cochrane Risk of Bias tool, which evaluates bias arising from randomization, deviations from intended interventions, missing outcome data, outcome measurement, and selective reporting.¹² Any discrepancies were resolved through consensus.

Endpoints and outcome definitions

Primary angiographic end points included adequate occlusion, complete occlusion, residual neck, residual aneurysm, aneurysm recurrence, and major recurrence. Adequate occlusion was defined as either complete occlusion or neck remnant at follow-up imaging. When studies reported angiographic results using the Raymond–Roy occlusion classification, complete occlusion corresponded to class I, neck remnant to class II, and residual aneurysm to class III.^{13,14} In studies that did not explicitly apply the Raymond–Roy classification, angiographic outcomes were extracted according to each study's original definitions and subsequently mapped to equivalent categories whenever possible to enable pooled analyses. To ensure outcome harmonization without introducing bias, the authors' original definitions were strictly followed, and raw event counts were used exactly as reported, avoiding any post-hoc reclassification of the original angiographic data. Angiographic outcomes were assessed at two time points, when available: immediate postprocedural imaging and the last available angiographic follow-up.

Safety outcomes were analyzed as a distinct end point category and included procedure-related complications, neurologic outcomes, all-cause mortality, and retreatment. Procedure-related complications encompassed thromboembolic events, intraprocedural rupture, hemorrhagic complications, ischemic stroke, and other adverse events as defined by the individual trials. Given the potential variability in safety reporting across different centers and eras, adverse events were classified by grouping them into these broad procedural categories exactly as adjudicated by the original study investigators. Complications were analyzed as overall procedural complication rates. Favorable functional outcome was defined as a modified Rankin Scale (mRS) score of 0–2 at the longest reported clinical follow-up. Poor functional outcome was defined as an mRS score of 3–5, when available. Mortality was analyzed as all-cause mortality during the reported follow-up period.

Statistical analysis

Pooled estimates were calculated using a random-effects model to account for between-study heterogeneity. Effect sizes for dichotomous outcomes were expressed as risk ratios (RRs) with corresponding 95% confidence intervals (CIs). Random-effects pooling was performed using the inverse-variance method with restricted maximum likelihood estimation of between-study variance, and CIs were calculated using the Hartung–Knapp–Sidik–Jonkman approach. Statistical heterogeneity across studies was assessed using both the Cochran Q test and the I^2 statistic. A P value < 0.05 for the Cochran Q test was considered indicative of statistically significant heterogeneity, whereas I^2 values $> 50\%$ were interpreted as reflecting substantial heterogeneity. Assessment of publication bias was considered; however, due to the limited number of included studies ($n = 6$), formal evaluation using funnel plot asymmetry and Egger's test was not performed.

To evaluate the robustness of the pooled estimates and explore potential sources of heterogeneity, leave-one-out sensitivity analyses were conducted by sequentially excluding each study and recalculating the pooled effect estimates. For continuous outcomes such as packing density, when studies reported medians and interquartile ranges rather than means and standard deviations, summary statistics were converted to means using established distribution-based methods. Specifically, the quantile estimation and Box–Cox transformation methods were applied to estimate means and variances from reported medians, enabling inclusion of these data in pooled analyses.¹⁵ All statistical analyses were performed using R software (version 4.2.3; R Foundation for Statistical Computing, Vienna, Austria). A P value < 0.05 was considered statistically significant.

Results

Literature review

A total of 108 records were identified through database searching, including MEDLINE (via PubMed) ($n = 22$), Scopus ($n = 43$), and Web of Science ($n = 43$). After the removal of 52 duplicate records, 56 records remained and were screened based on titles and abstracts. Following the initial screening, 48 records were excluded because they were case reports, reviews, non-randomized studies, or not relevant to the research question. Subsequently, eight reports were sought for

retrieval; all were successfully retrieved and assessed for eligibility. No additional records were identified through other sources. After full-text assessment, two reports were excluded: one non-randomized study and one study not relevant to the topic of interest. Ultimately, six RCTs^{4–8,16} were included in the final review and meta-analysis. The study selection process is summarized in Figure 1.

Patient population and study characteristics

Across the included RCTs, six studies contributed patient-level and aneurysm-level data comparing HGCs with BPCs. Overall, 2,486 patients with 2,513 treated intracranial aneurysms were included. Patient age was reported in most studies, with mean or median ages generally ranging from the early 50s to the mid-60s. A consistent female predominance was observed across both treatment groups, with women comprising approximately 65%–75% of the study populations.

Regarding aneurysm location, data from five studies demonstrated a predominance of anterior circulation aneurysms in both treatment arms. Specifically, the HGCs group included 762 anterior circulation aneurysms and 251 posterior circulation aneurysms, with 5 aneurysms classified as other locations or having missing location data. Similarly, the BPCs group comprised 750 anterior circulation aneurysms and 259 posterior circulation aneurysms, with 4 aneurysms categorized as other locations or having missing location data. The most frequently treated locations across both groups were the internal carotid artery (663/1,512), the middle cerebral artery (167/1,512), the anterior communicating artery (134/1,512), and the posterior communicating artery (104/1,512). Posterior circulation aneurysms were less common and most frequently involved the basilar and vertebrobasilar arteries (Table 1).

Immediate angiographic outcomes

Immediate complete occlusion did not differ significantly between HGCs and BPCs (RR: 0.87; 95% CI, 0.70–1.09; I^2 : 63.0%; P_{het} : 0.019, $P = 0.173$), nor did immediate adequate occlusion (RR: 0.96; 95% CI, 0.85–1.07; I^2 : 31.0%; P_{het} : 0.214, $P = 0.334$). Rates of immediate residual neck were also similar between HGCs and BPCs (RR: 0.94; 95% CI, 0.67–1.32; I^2 : 44.8%; P_{het} : 0.123, $P = 0.656$).

In contrast, immediate residual aneurysm was significantly more frequent with HGCs than with BPCs (RR: 1.12; 95% CI, 1.01–1.24; I^2 : 0.0%; P_{het} : 0.806, $P = 0.041$). Mean packing

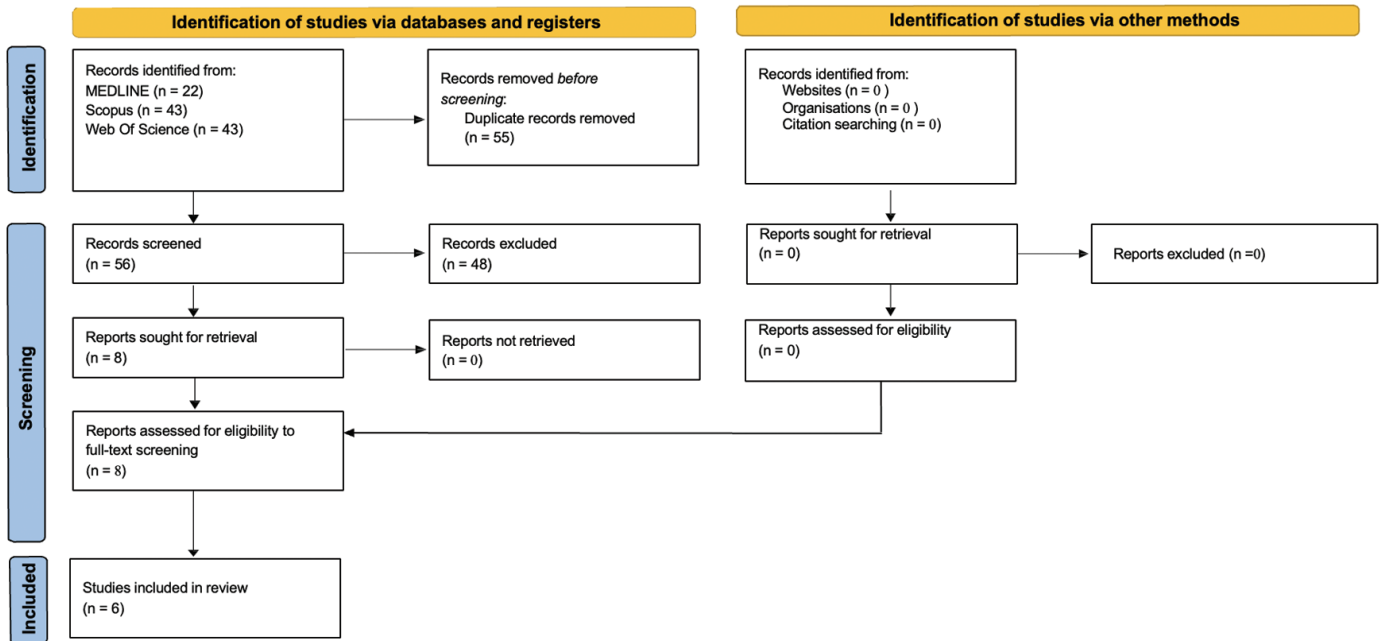


Figure 1. PRISMA flow diagram.

density did not differ significantly between HGCs and BPCs (mean difference: 19.13; 95% CI, -3.28 to 41.55; $P_{\text{het}} < 0.001$), although substantial heterogeneity was present (I^2 : 98.4%) (Figure 2).

Angiographic outcomes at last follow-up

At the last angiographic follow-up, HGCs demonstrated a trend toward higher complete occlusion rates than BPCs, although the difference did not reach statistical significance (RR: 1.21; 95% CI, 0.99–1.49; I^2 : 54.1%; P_{het} : 0.088, $P = 0.058$). Adequate occlusion rates at the last follow-up were comparable between HGCs and BPCs (RR: 1.08; 95% CI, 0.92–1.28; I^2 : 14.6%; P_{het} : 0.465, $P = 0.179$), as were residual neck rates (RR: 0.74; 95% CI, 0.32–1.72; I^2 : 23.3%; P_{het} : 0.271, $P = 0.267$).

Notably, residual aneurysm at the last follow-up was significantly less frequent with HGCs than with BPCs (RR: 0.75; 95% CI, 0.68–0.83; I^2 : 0.0%; P_{het} : 0.953, $P = 0.006$) (Figure 3).

Safety outcomes

Functional outcomes were comparable between HGCs and BPCs, with no significant differences in favorable functional outcome (mRS score: 0–2) (RR: 0.98; 95% CI, 0.95–1.01; I^2 : 0.0%; P_{het} : 0.718, $P = 0.145$) or poor functional outcome (mRS score: 3–5) (RR: 1.10; 95% CI, 0.58–2.07; I^2 : 0.0%; P_{het} : 0.475, $P = 0.672$). In contrast, major recurrence occurred significantly less frequently with HGCs than with BPCs (RR: 0.71; 95% CI, 0.54–0.94;

I^2 : 15.6%; P_{het} : 0.315, $P = 0.024$). No significant differences were observed between HGCs and BPCs in retreatment rates or mortality.

Retreatment rates did not differ significantly between HGCs and BPCs (RR: 0.79; 95% CI, 0.50–1.25; I^2 : 6.1%; P_{het} : 0.377, $P = 0.244$). Mortality was also comparable between HGCs and BPCs (RR: 0.78; 95% CI, 0.26–2.29; I^2 : 40.6%; P_{het} : 0.150, $P = 0.552$). Overall procedural complication rates were comparable, with no significant difference between HGCs and BPCs (RR: 0.96; 95% CI, 0.69–1.34; I^2 : 28.7%; P_{het} : 0.219, $P = 0.782$) (Figure 4, Table 2). Complication details are presented in Supplementary Table 2.

Heterogeneity and quality assessment

For complete occlusion at the last follow-up, a leave-one-out sensitivity analysis demonstrated that omission of the study by Poncyjusz et al.¹⁶ reduced heterogeneity to I^2 : 0% while preserving the direction of the pooled effect estimate. Similarly, for immediate complete occlusion, exclusion of individual studies reduced heterogeneity to below 50% without materially altering the pooled RR. In contrast, substantial heterogeneity persisted for packing density (I^2 : 98.4%), and leave-one-out analyses showed that removal of any single study did not meaningfully reduce heterogeneity or materially change the pooled mean difference. These findings suggest that the observed heterogeneity in packing density reflects true between-study

variability, including differences in measurement methodology, aneurysm morphology, and procedural or device-related factors, rather than disproportionate influence from a single study (Supplementary Figure 1).

Risk of bias was assessed using the RoB 2.0 framework, and the results are summarized in Supplementary Figure 2. Across the six included RCTs, four were judged to be at low overall risk of bias, one raised some concerns, and one was classified as having a high risk of bias. The most frequent sources of potential bias were related to deviations from intended interventions (Domain 2) and selection of the reported result (Domain 5), whereas bias arising from the randomization process (Domain 1), missing outcome data (Domain 3), and outcome measurement (Domain 4) was generally low across studies (Supplementary Figure 2).

Discussion

In this meta-analysis of six RCTs including more than 2,400 patients and 2,500 treated aneurysms, we found that HGCs provided improved long-term angiographic durability compared with BPCs while maintaining comparable immediate angiographic, safety, and clinical outcomes. Specifically, although immediate complete and adequate occlusion rates were similar between HGCs and BPCs, HGCs were associated with significantly lower rates of residual aneurysm at the

Table 1. Baseline characteristics of the patients

| Study | n patients | n aneurysms | Morphology | Mean age | Male/female ratio | Aneurysm status (ruptured/unruptured) | Location | Mean size | Mean radiologic follow-up (months) | Mean clinical follow-up (months) |
|---|----------------------|----------------------|--|-------------------------|--|---------------------------------------|---|------------------------------|------------------------------------|----------------------------------|
| Imamura et al., ⁸ (Japan) | HGC (214), BPC (211) | HGC (214), BPC (211) | N/A | HGC (63.2), BPC (63.3) | HGC [66 M (30.8%)/148 F (69.2%)]; BPC [50 M (33.7%)/161 F (76.3%)] | HGC (8 R/206 U), BPC (8 R/203 U) | HGC (ICA: 144; MCA: 28; ACA: 6; VABA: 35; Other: 1); BPC (ICA: 134; MCA: 28; ACA: 3; VABA: 45; Other: 1) | HGC (8 mm), BPC (8.2 mm) | 12 months | 12 months |
| Bendok et al., ⁴ (USA and Canada) | HGC (282), BPC (291) | HGC (297), BPC (303) | HGC (Bifurcation: 156; Sidewall: 86; Terminal: 44), BPC (Bifurcation: 141; Sidewall: 107; Terminal: 44) | HGC (56.5), BPC (56.9) | HGC [59 M (19.87%)/238 F (80.13%)]; BPC [67 M (22.11%)/236 F (77.89%)] | HGC (76 R/216 U), BPC (93 R/208 U) | HGC (ACA: 10; ACom: 70; Basilar: 35; ICA: 76; MCA: 39; PCom: 51; Vertebral: 5); BPC (ACA: 7; ACom: 64; Basilar: 34; ICA: 99; MCA: 29; PCom: 53; Vertebral: 5) | HGC (7.30 mm), BPC (7.50 mm) | N/A* | N/A* |
| Poncyliusz et al., ¹⁶ (Poland) | HGC (50), BPC (46) | HGC (50), BPC (46) | HGC (Bifurcation: 20; Segment of an artery: 30), BPC (Bifurcation: 23; Segment of an artery: 23) | HGC (49.6), BPC (52.17) | HGC [19 M (38%)/31 F (62%)]; BPC [16 M (34.78%)/30 F (65.22%)] | HGC (0 R/50 U), BPC (0 R/46 U) | HGC (Anterior circulation: 38; Posterior circulation: 12), BPC (Anterior circulation: 37; Posterior circulation: 9) | HGC (8.32 mm), BPC (8.43 mm) | 12 months | 12 months |
| Taschner et al., ⁶ (France and Germany) | HGC (239), BPC (237) | HGC (239), BPC (237) | HGC [Regular: 136 (56%); Irregular/lobulated: 107 (44%)], BPC [Regular: 133 (55%); Irregular/lobulated: 107 (45%); Missing: 1] | HGC (52.9), BPC (54.1) | HGC [71 M (29.22%)/172 F (70.78%)]; BPC [80 M (33.20%)/161 F (66.80%)] | HGC (103 R/140 U), BPC (105 R/136 U) | HGC [Anterior: 177 (74%); Posterior/other: 62 (26%); Missing: 4], BPC [Anterior: 182 (76%); Posterior/other: 56 (24%); Missing: 3] | HGC (6.8 mm), BPC (7.1 mm) | 18 months | 18 months |
| White et al., ⁵ (UK, USA, Brazil, Germany, Australia, France, Argentina) | HGC (234), BPC (235) | HGC (234), BPC (235) | HGC (Irregular/multilobulated: 76), BPC (Irregular/multilobulated: 77) | N/A | HGC [73 M (29.32%)/176 F (70.68%)]; BPC [76 M (30.40%)/174 F (69.60%)] | HGC (139 R/110 U), BPC (13 R/112 U) | N/A | Mean 6.5 mm (overall) | N/A | 18 months |
| Raymond et al., ⁷ (USA, Canada, UK, France, Chile, Japan) | HGC (225), BPC (222) | HGC (225), BPC (222) | N/A | HGC (58), BPC (57) | HGC [60 M (26.67%)/165 F (73.33%)]; BPC [68 M (30.63%)/154 F (69.37%)] | HGC (40 R/185 U), BPC (39 R/183 U) | HGC (ICA: 109; ACA: 42; MCA: 23; Basilar: 32; Other Post: 19); BPC (ICA: 101; ACA: 44; MCA: 20; Basilar: 44; Other Post: 13) | HGC (10.7 mm), BPC (11.3 mm) | 18 months | 18 months |

*Bendok et al.⁴ did not report radiological or clinical follow-up data; therefore, follow-up duration could not be extracted for this study. HGC, hydrogel-coated coil; BPC, bare platinum coil; ICA, internal carotid artery; MCA, middle cerebral artery; ACA, anterior cerebral artery; VABA, vertebrobasilar artery; PCom, posterior communicating artery; ACom, anterior communicating artery; R, ruptured; U, unruptured; M, male; F, female; N/A, not applicable.

Angiographic Outcomes (Immediate)

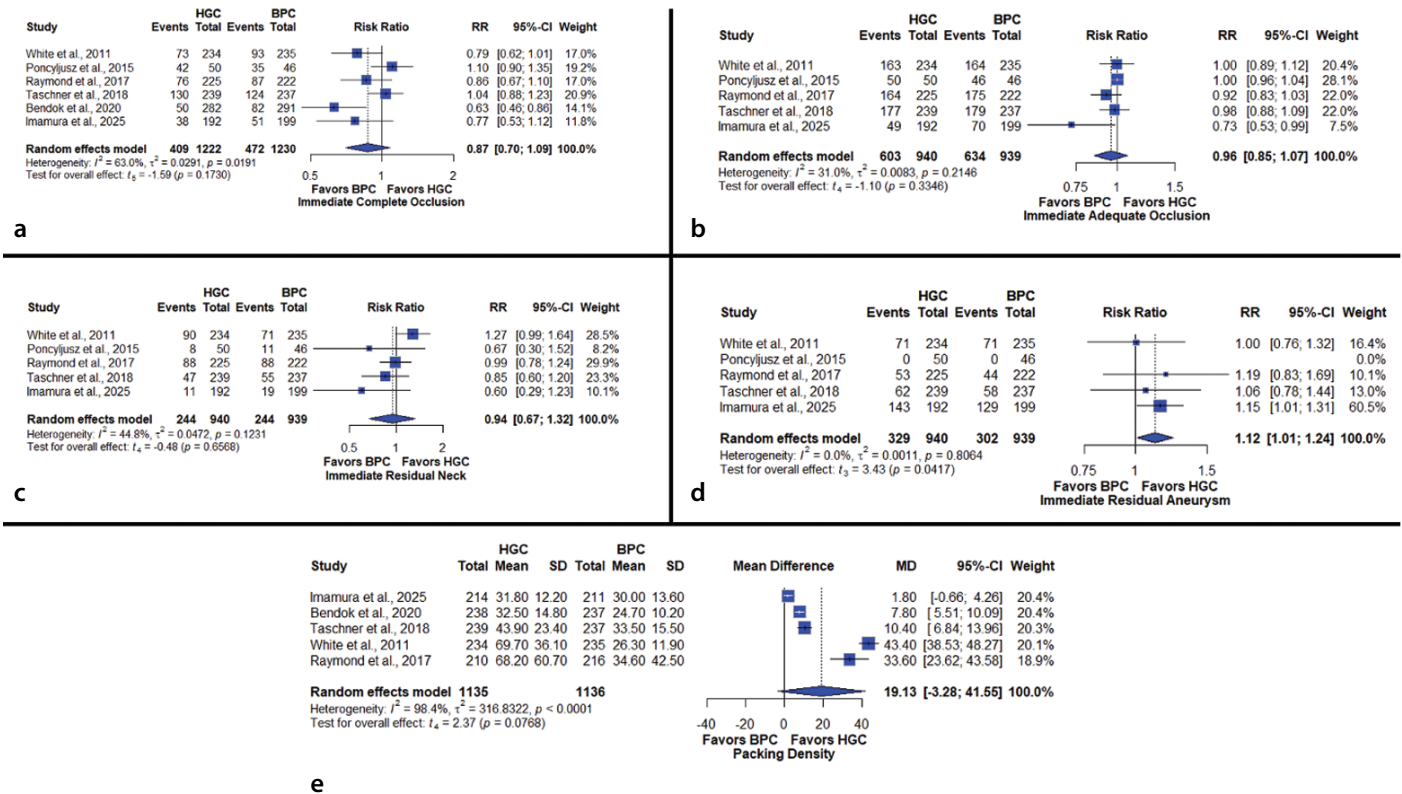


Figure 2. Forest plots showing pooled estimates comparing HGCs with BPCs for angiographic outcomes assessed immediately after the procedure: (a) immediate complete occlusion, (b) immediate adequate occlusion, (c) immediate residual aneurysm, (d) immediate residual neck, and (e) packing density. HGC, hydrogel-coated coils; BPC, bare platinum coil.

Angiographic Outcomes (Last Follow-up)

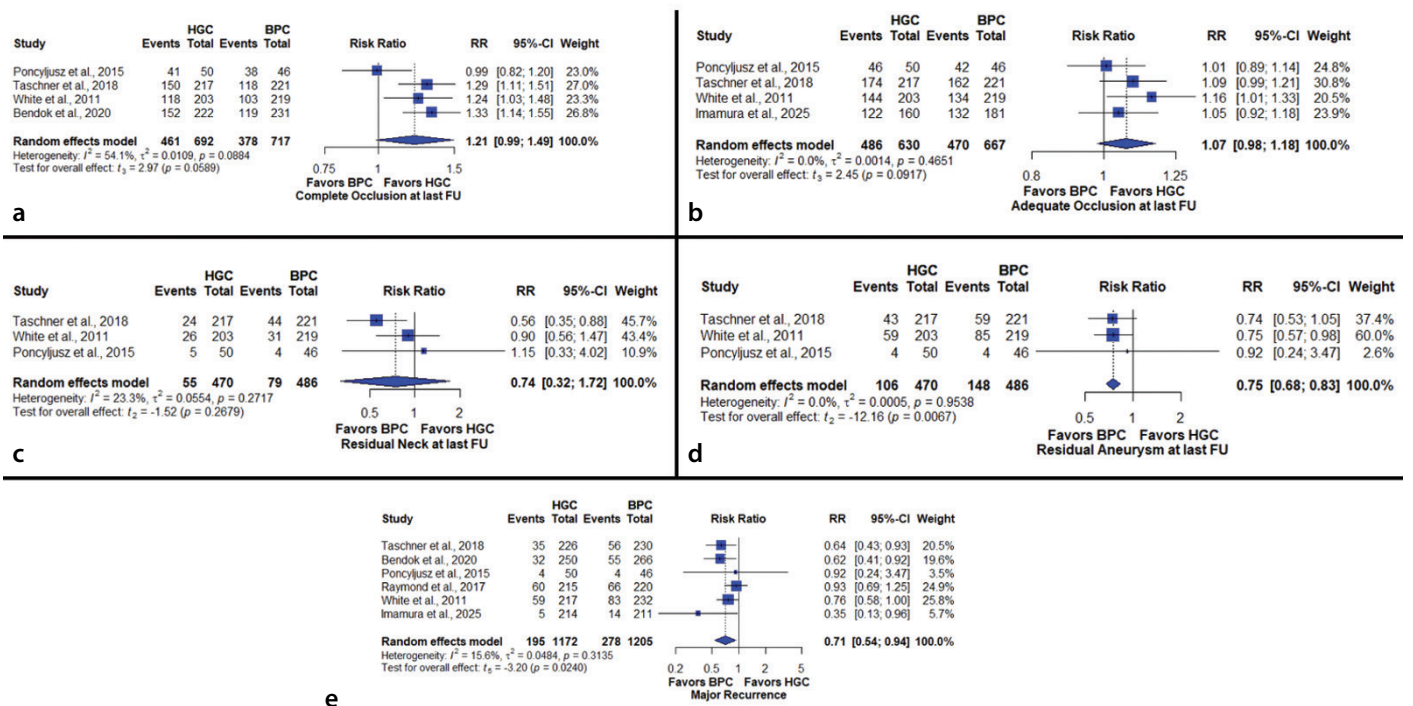


Figure 3. Forest plots showing pooled estimates comparing HGCs with BPCs for angiographic outcomes assessed at the last available follow-up: (a) complete occlusion, (b) adequate occlusion, (c) residual aneurysm, (d) residual neck, and (e) major recurrence. HGC, hydrogel-coated coils; BPC, bare platinum coil.

Safety Outcomes

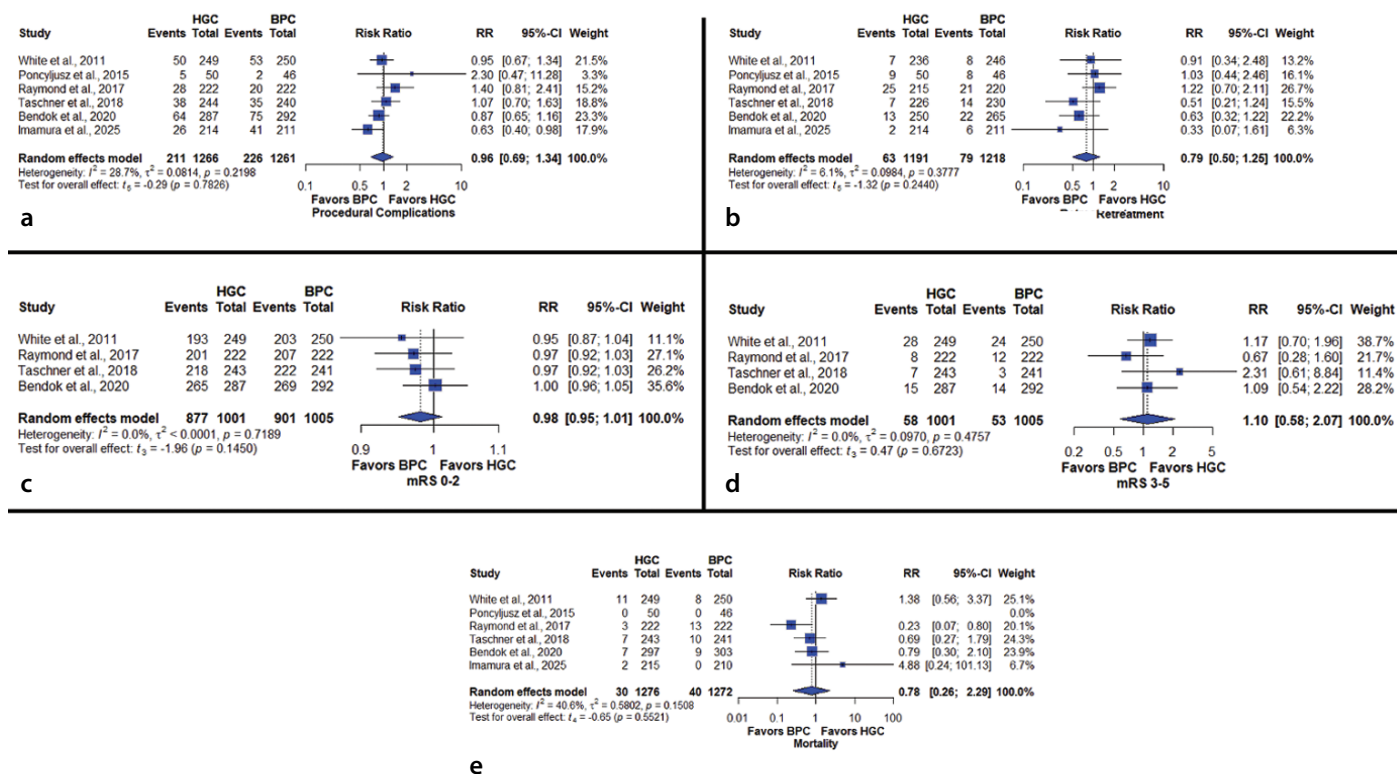


Figure 4. Forest plots showing pooled estimates comparing HGCs with BPCs for safety and clinical outcomes: (a) procedural complications, (b) favorable functional outcome (mRS score: 0–2), (c) poor functional outcome (mRS score: 3–5), (d) retreatment, and (e) all-cause mortality. HGC, hydrogel-coated coils; BPC, bare platinum coil; mRS, modified Rankin Scale.

| End point | Estimate (95% CI) | I ² (%) | Number of studies | Number of events/total | P value | |
|---|-------------------------------|----------------------|-------------------|-----------------------------------|---|--------------|
| Angiographic outcomes (immediate) | Immediate complete occlusion | 0.87 (0.70; 1.09) | 63.0% | 6 | HGC: 409/1,222 vs. BPC: 472/1,230 | 0.173 |
| | Immediate adequate occlusion | 0.96 (0.85; 1.07) | 31.0% | 5 | HGC: 603/940 vs. BPC: 634/939 | 0.334 |
| | Immediate residual neck | 0.94 (0.67; 1.32) | 44.8% | 5 | HGC: 244/940 vs. BPC: 244/939 | 0.656 |
| | Immediate residual aneurysm | 1.12 (1.01; 1.24) | 0.0% | 5 | HGC: 329/940 vs. BPC: 302/939 | 0.041 |
| | Packing Density | 19.13 (–3.28; 41.55) | 98.4% | 5 | Total participants: HGC: 1,135 vs. BPC: 1,136 | 0.076 |
| Angiographic outcomes (last follow-up) | Complete occlusion at last FU | 1.21 (0.99; 1.49) | 54.1% | 4 | HGC: 461/692 vs. BPC: 378/717 | 0.058 |
| | Adequate occlusion at last FU | 1.08 (0.92; 1.28) | 14.6% | 3 | HGC: 364/470 vs. BPC: 338/486 | 0.179 |
| | Residual neck at last FU | 0.74 (0.32; 1.72) | 23.3% | 3 | HGC: 55/470 vs. BPC: 79/486 | 0.267 |
| | Residual aneurysm at last FU | 0.75 (0.68; 0.83) | 0.0% | 3 | HGC: 106/470 vs. BPC: 148/486 | 0.006 |
| Safety outcomes | Major recurrence | 0.71 (0.54; 0.94) | 15.6% | 6 | HGC: 195/1,172 vs. BPC: 278/1,205 | 0.024 |
| | mRS 0–2 | 0.98 (0.95; 1.01) | 0.0% | 4 | HGC: 877/1,001 vs. BPC: 901/1,005 | 0.145 |
| | mRS 3–5 | 1.10 (0.58; 2.07) | 0.0% | 4 | HGC: 58/1,001 vs. BPC: 53/1,005 | 0.672 |
| | Retreatment | 0.79 (0.50; 1.25) | 6.1% | 6 | HGC: 63/1,191 vs. BPC: 79/1,218 | 0.244 |
| | Mortality | 0.78 (0.26; 2.29) | 40.6% | 6 | HGC: 30/1,276 vs. BPC: 40/1,272 | 0.552 |
| Procedural complications | 0.96 (0.69; 1.34) | 28.7% | 6 | HGC: 211/1,266 vs. BPC: 226/1,261 | 0.782 | |

HGC, hydrogel-coated coils; BPC, bare platinum coils; FU, follow-up; mRS, modified Rankin Scale.

last follow-up and a lower incidence of major recurrence than BPCs. Importantly, these angiographic benefits did not translate into differences in functional outcomes, retreatment rates, procedural complications, or mortality, underscoring a favorable balance between durability and safety.

The absence of a statistically significant difference in immediate angiographic outcomes aligns with the biological premise that hydrogel expansion and healing-related effects are not expected to manifest immediately after coil deployment.¹⁷ Initial occlusion after endovascular coiling is largely determined by mechanical factors, including coil framing, aneurysm morphology, and operator technique.^{6,18-20} Our finding that immediate complete occlusion and adequate occlusion were comparable between HGCs and BPCs is consistent with observations from prior randomized trials, including HELPS,⁵ HEAT,⁴ and GREAT,⁶ in which early angiographic end points were not consistently superior with hydrogel technology. The higher rate of immediate residual aneurysm observed with HGCs than with BPCs may reflect a deliberate procedural strategy favoring progressive thrombosis rather than aggressive immediate packing, particularly in the context of coils designed to expand and remodel over time.

In contrast, the advantages of HGCs became evident at follow-up, with significantly lower residual aneurysm rates than with BPCs and a strong trend toward higher complete occlusion rates. These findings support the concept of aneurysm occlusion as a dynamic biological process rather than a static procedural end point. The reduction in residual aneurysm and major recurrence rates observed in our analysis is consistent with experimental and clinical evidence suggesting that hydrogel expansion enhances volumetric filling, stabilizes intra-aneurysmal thrombus, and promotes neointimal formation at the aneurysm neck. The HYBRID trial,⁸ in particular, introduced a longitudinal framework for evaluating angiographic evolution and demonstrated increased thrombosis and reduced progression to body filling with HGCs compared with BPCs, even though the difference in binary recanalization rates was not statistically significant. Our meta-analysis extends these findings by confirming that such favorable occlusion trajectories translate into measurable reductions in residual aneurysm and major recurrence across randomized data.

The discrepancy between improved angiographic durability and unchanged clinical

outcomes merits careful consideration. Functional outcomes following aneurysm treatment are influenced by multiple factors beyond angiographic appearance, including aneurysm rupture status, baseline neurologic condition, periprocedural complications, and comorbidities. Given the relatively low absolute event rates for retreatment, rebleeding, and aneurysm-related mortality after modern coil embolization, larger sample sizes and longer follow-up periods may be required to detect clinically meaningful differences attributable solely to coil technology.

Despite lower recurrence rates with HGCs than with BPCs (RR: 0.71; $P = 0.024$), retreatment rates did not differ significantly between the two groups (RR: 0.79; $P = 0.244$). This apparent discrepancy may reflect variability in retreatment thresholds across centers and time periods, as well as the fact that not all angiographic recurrences are clinically significant or require reintervention. Retreatments are influenced by multiple factors, including aneurysm characteristics, patient-related risk, and procedural considerations, which may weaken the direct relationship between recurrence and retreatment. Additionally, the relatively low event rate and differences in follow-up duration across studies may have limited the ability to detect significant differences in retreatment outcomes.

Packing density remains a contentious surrogate marker of long-term aneurysm occlusion. Although HGCs are designed to increase effective volumetric filling, our analysis did not demonstrate a statistically significant difference in mean packing density between HGCs and BPCs, and heterogeneity remained substantial despite sensitivity analyses. This likely reflects variability in packing density calculation methods, aneurysm geometry, and coil selection strategies across trials rather than true biological inconsistency. Moreover, the relationship between packing density and durable occlusion is complex and nonlinear, and emerging evidence suggests that coil composition, thrombus organization, and neck healing may be at least as important as absolute packing metrics.^{4,10} Thus, packing density alone may be an insufficient explanatory variable for the observed durability benefits of hydrogel technology.

Despite demonstrating improved long-term angiographic durability, the limited adoption of HGCs in routine clinical practice likely reflects a mismatch between their principal benefit and the outcomes that most

strongly guide day-to-day treatment decisions. In contemporary endovascular workflows, procedural success is primarily judged by immediate angiographic results and short-term safety, domains in which HGCs do not consistently outperform BPCs. In contrast, the advantages of hydrogel technology emerge gradually through improved occlusion trajectories, reduced residual aneurysm formation, and lower major recurrence rates than with BPCs, benefits that are not immediately apparent at the time of treatment and may not translate into early clinical differences. Concurrently, the widespread adoption of flow diverters^{21,22} and intrasaccular devices (e.g., WEB and ARTISSE)^{23,24} has reshaped treatment paradigms by offering greater durability advantages in selected aneurysm subtypes, thereby reducing reliance on coil-based optimization alone. As a result, HGCs are no longer used as the default embolization device but may have a more selective role in contemporary practice, particularly for aneurysms at higher risk of long-term recurrence. Importantly, coil embolization remains a cornerstone of aneurysm treatment, especially for ruptured aneurysms or when parent vessel reconstruction is undesirable, and in this setting, HGCs may serve as a durability-enhancing adjunct without additional safety concerns. The present findings suggest that the relative underutilization of hydrogel technology reflects evolving therapeutic priorities rather than a lack of biological or angiographic efficacy, supporting its continued consideration when long-term angiographic stability is prioritized.

Heterogeneity across outcomes was generally modest and was largely attributable to individual trials in sensitivity analyses, particularly for complete occlusion end points. The reduction in heterogeneity after omission of specific studies suggests methodological and population-level differences rather than instability of the overall findings.

Several limitations warrant acknowledgment. The small number of included studies ($n = 6$) precluded a reliable assessment of publication bias, as commonly used methods such as funnel plots and Egger's test are considered unreliable when fewer than 10 studies are available. Therefore, the presence of publication bias cannot be excluded. Although this meta-analysis includes all available randomized evidence to date, the total number of trials remains limited, and follow-up durations were predominantly restricted to 12–18 months. Longer-term angiographic and clinical outcomes beyond 2 years remain incompletely characterized. Ad-

ditionally, differences in aneurysm selection, adjunctive device use, and operator preference across trials may influence generalizability. Finally, evolving coil technology and procedural techniques may further modify outcomes in contemporary practice.

In conclusion, this post-HYBRID updated meta-analysis demonstrates that HGCs confer superior long-term angiographic durability compared with BPCs, as reflected by lower residual aneurysm and major recurrence rates, while maintaining comparable safety and clinical outcomes. These findings reinforce the concept that biologically active coil technologies can favorably influence aneurysm healing over time and support the continued use of HGCs as a durability-enhancing option in endovascular aneurysm treatment.

Footnotes

Conflict of interest disclosure

The authors declared no conflicts of interest.

Supplementary Figures Link: <https://d2v96fxpocvxx.cloudfront.net/17d041fe-057c-4c8e-a75d-948e33c0152a/content-images/4b59de94-1c8f-47d6-8efa-e8ce62bd4a7a.pdf>

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