Placental-derived Membrane Augmentation in Anterior Cruciate Ligament Reconstruction: A Systematic Review of Clinical and Imaging Outcomes

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Background

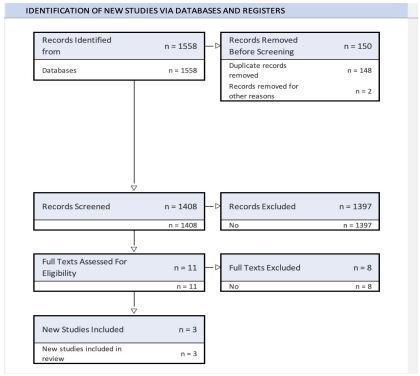
- Placental-derived membrane products (amnion, amnion/chorion, umbilical cord–derived tissues) are used as biologic adjuncts during ACL reconstruction to potentially modulate inflammation and accelerate graft maturation.
- Despite increasing adoption, the clinical evidence base—particularly imaging-defined graft maturation, patient-reported outcomes, and return-to-sport endpoints—remains unclear.
- **Objective**: Systematically review clinical and imaging outcomes after placental-derived membrane augmentation in ACLR.

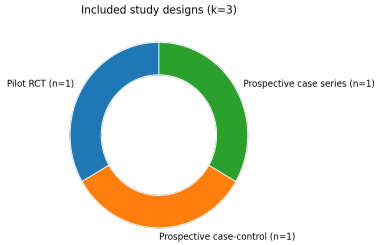
Methods

- **Design:** PRISMA 2020–compliant systematic review (PROSPERO registered); Level of Evidence IV.
- **Registration:** PROSPERO CRD420251072924.
- **Databases:** PubMed/MEDLINE, Embase, Scopus, Web of Science (Inception → June 12, 2025).
- **Records identified:** 1,558 (PubMed 42; Embase 327; Web of Science 44; Scopus 1,145).
- **Screening:** Two reviewers independently screened, extracted data, and assessed risk of bias (RoB 2 for RCT; Newcastle–Ottawa for observational).
- **Synthesis:** No meta-analysis (non-overlapping outcomes/time points; heterogeneous interventions).

Results

- **k= 3 studies | N=87 | 1 pilot RCT | No overall benefit after 24 months**
- **Inclusion:** 3 prospective studies (1 pilot RCT, 1 case-control, 1 case series), N=87.
- **Interventions:** Heterogeneous (amnion wrap + BMAC; amnion/chorion wrap; umbilical cord wrap).
- **Imaging:** Pilot RCT: no MRI maturation differences through 24 months.
- **PROMs:** Observational studies: possible early PROM/MRI signals (~6 months), but high RoB/incomplete follow-up.
- **Safety:** No major adverse events reported.

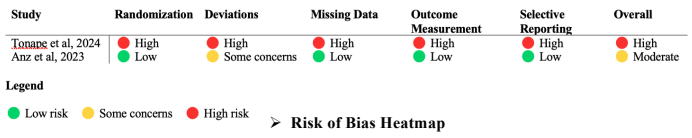




- **Included study designs (k=3):**

1 pilot RCT, 1 prospective case-control study, and 1 prospective case series (total N=87).

- **2020 PRISMA Flow Diagram**



- **Risk of Bias Heatmap**

Conclusions

- Current clinical evidence supporting placental-derived membrane augmentation in ACLR is limited (k=3), heterogeneous, and not meta-analyzable.
- One pilot randomized trial demonstrated no detectable benefit at 2 years, while lower-quality observational evidence suggests possible early improvements in selected outcomes.
- Routine adoption cannot be recommended without adequately powered, standardized trials with prespecified imaging protocols and validated return-to-sport criteria.

Discussion

- **Key limitations**: small study sizes, heterogeneous biologic products and co-interventions (e.g., BMAC), variable rehab and outcome timing, and inconsistent adverse-event reporting.
- Future trials should standardize graft type, membrane product handling, rehabilitation, and imaging endpoints (MRI sequences/time points), and include prespecified RTS criteria and failure definitions.
- **Clinical takeaway**: Interpret early observational signals cautiously; prioritize high-quality comparative evidence before expanding use.

Clinical Relevance

- Evidence is limited to 3 small prospective studies (87 patients) with heterogeneous products and outcomes.
- The best available evidence (pilot RCT) showed no MRI or PROM benefit through 24 months.
- Observational studies suggest possible early PROM/MRI improvements but carry high risk of bias.
- **Recommendation**: Use selectively (if at all) and counsel patients that benefits are unproven pending adequately powered trials.

References

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