

Extracellular Matrix Biomaterials and Contemporary Strategies for The Prevention and Management of Postoperative Seroma: A Qualitative Integrative Analysis of Surgical, Regenerative, And Wound-Healing Evidence

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Abstract: Background: Postoperative seroma remains one of the most persistent and clinically frustrating complications across multiple surgical specialties, particularly breast surgery, ventral hernia repair, reconstructive procedures, orthopedic interventions, and complex wound care. Although often treated as a minor sequela, seroma formation may produce pain, delayed healing, repeated aspirations, anxiety, prolonged follow-up, infection risk, and in some cases chronic encapsulated fluid collections that require reoperation. At the same time, regenerative biomaterials derived from decellularized extracellular matrix have emerged as a potentially important adjunct in tissue remodeling, dead-space control, inflammatory modulation, and wound repair. The present study develops an original qualitative integrative analysis based strictly on the supplied reference set.

Objective: To synthesize current knowledge on postoperative seroma pathogenesis, classification, prevention, and management, with particular emphasis on the theoretical and practical role of extracellular matrix-based biologic scaffolds in reducing seroma burden and improving tissue healing.

Methods: A qualitative integrative research design was used. Fifteen provided references were analyzed through comparative thematic synthesis. Sources included surveys, case reports, classification studies, experimental animal work, regenerative medicine reviews, wound-healing studies, and clinical reports. The analysis focused on four domains: mechanisms of seroma formation, limitations of conventional management, principles of extracellular matrix scaffold biology, and translational applications of biomaterials in seroma-prone surgical settings.

Results: The evidence indicates that seroma is best understood as a multifactorial consequence of surgical dead space, disrupted lymphatics, inflammatory exudation, biomechanical shear, and impaired tissue adherence. Existing management strategies remain variable and often reactive. Classification systems improve conceptual precision but are not yet universally integrated into management pathways. Biologic scaffolds appear promising because they do not merely fill tissue deficits; they may also influence host response, recruit progenitor cells, support constructive remodeling, and alter the chronicity of fluid-producing tissue planes. Evidence from preclinical models, wound-care applications, and selected clinical cases supports a rationale for biomaterial-assisted seroma management, though robust comparative trials remain limited.

Conclusion: Seroma management should move from passive drainage-centered thinking toward biologically informed tissue remodeling strategies. Extracellular matrix biomaterials offer a compelling translational framework, but high-quality prospective research is required to define indications, timing, cost-effectiveness, and procedure-specific protocols.

Keywords: Postoperative seroma, extracellular matrix, biologic scaffolds, wound healing, regenerative surgery,

mastectomy, ventral hernia repair.

Introduction: Postoperative seroma continues to occupy an unusual place in surgical literature and clinical practice. It is common enough to be expected, troublesome enough to alter outcomes, and inconsistent enough to resist a universally accepted management algorithm. In many operative settings, seroma is described almost casually, as though it were merely a transient accumulation of clear fluid within a postoperative cavity. Yet the references provided collectively demonstrate that seroma should not be dismissed as an innocuous byproduct of surgery. It is a dynamic postoperative event shaped by lymphatic disruption, inflammatory signaling, tissue dissection, dead-space persistence, mechanical motion, wound environment, and host response (Kazzam & Ng, 2023; Morales-Conde, 2012). When persistent, recurrent, delayed, or complex, it can profoundly interfere with recovery, increase healthcare contact, complicate reconstruction, and, in selected cases, evolve into a chronic problem requiring more invasive intervention (Ghazal et al., 2022; Mohamed et al., 2016).

The burden of seroma extends beyond surgical inconvenience. In breast surgery, especially mastectomy and axillary procedures, seroma can delay adjuvant planning, prolong drainage, increase outpatient aspirations, and affect patient satisfaction. Fairhurst et al. (2024) show that even in a high-resource national surgical environment, significant variation persists in the use of drains and postoperative seroma management after mastectomy and axillary surgery. Such variability is not merely administrative; it reflects deeper uncertainty about mechanism, prevention, and optimal intervention. If practices remain heterogeneous among experienced clinicians, then the field has not yet achieved conceptual maturity.

In ventral hernia repair, the problem becomes even more layered. Morales-Conde (2012) argued for a classification system after laparoscopic ventral hernia repair, indicating that seroma is not a single clinical entity but a spectrum with differing relevance and implications. Petro et al. (2016), in designing a ventral hernia staging system, further reinforced the need to understand postoperative complications through structured frameworks rather than anecdotal impressions. The practical implication is clear: seroma should be approached as a phenomenon that can be staged, contextualized, and linked to surgical environment rather than viewed as a uniform complication.

The clinical challenge becomes sharper when seroma persists or becomes delayed. Ghazal et al. (2022)

reported treatment of persistent complex seroma after ventral incisional hernia repair with capsulectomy and scarification using argon beam coagulator, illustrating that chronic seroma may require intervention far beyond aspiration and observation. Mohamed et al. (2016) described delayed onset seroma appearing five years after ventral incisional hernia repair, an observation that fundamentally disrupts the assumption that seroma is only an early postoperative issue. This delayed presentation invites a broader conceptualization: postoperative tissue planes may retain latent instability long after apparent healing, and biomaterial-tissue interactions, mechanical factors, or chronic inflammatory microenvironments may contribute to late fluid collection.

The references also open a second major theme: the potential relevance of extracellular matrix-based biologic scaffolds and regenerative biomaterials in addressing seroma-prone tissues. At first glance, the literature on extracellular matrix scaffolds may seem more applicable to chronic wounds, trauma, or tissue loss than to seroma. However, a deeper reading suggests an important convergence. Badylak (2014) described how decellularized allogeneic and xenogeneic tissues act as bioscaffolds whose function depends on host response. Beattie et al. (2009) demonstrated chemoattraction of progenitor cells by remodeling extracellular matrix scaffolds, supporting the idea that these materials can actively shape tissue regeneration rather than merely occupy space. Turner and Badylak (2014) highlighted the use of biologic scaffolds in chronic nonhealing wounds, emphasizing that scaffold-mediated healing involves complex interplay among structural support, signaling, cellular recruitment, and remodeling. These principles are highly relevant to seroma because seroma formation is intimately linked to the failure of tissue planes to re-adhere and remodel constructively after surgical disruption.

Clinical examples further strengthen this connection. Bettiol et al. (2021) reported a novel use of porcine bladder extracellular matrix scaffold to treat postoperative seroma in a total knee arthroplasty patient. Agalar et al. (2017) found in a rat model that porcine dermal collagen prevented seroma formation after mastectomy and axillary dissection. Diaz-Valadez et al. (2023) described clinical and histologic wound-healing responses with multi-tissue extracellular matrix and included cost comparison against negative pressure wound therapy. Valerio et al. (2015), Collins et al. (2023), and Kimmel (2018) discussed extracellular matrix or biomaterial-based approaches in trauma,

wound management, and cell signaling-focused healing applications. Individually, these studies are not identical in indication or design. Collectively, however, they point toward a biologically richer model of postoperative tissue management, one in which seroma prevention and treatment may be improved by guiding host remodeling rather than simply evacuating fluid.

This observation reveals the central literature gap addressed in the present article. Existing seroma literature often concentrates on immediate technical measures such as drains, compression, aspiration, and surgical revision, while biomaterial literature often focuses on regenerative reconstruction, chronic wounds, and soft-tissue restoration. The two bodies of knowledge have not been fully integrated into a unified theoretical framework for seroma prevention and management. The provided references suggest that such integration is overdue. Seroma is not solely a fluid problem. It is also a tissue-interface problem, an inflammatory problem, a dead-space problem, and a remodeling problem. Once seroma is reconceptualized in those terms, extracellular matrix biomaterials become relevant not as peripheral innovations but as potentially central tools in the future management of seroma-prone postoperative anatomy.

The present article therefore develops a publication-style original integrative analysis based strictly on the supplied references. The study does not claim new clinical trial data. Rather, it offers an original research-level synthesis by comparatively analyzing the evidence, identifying recurring mechanisms, evaluating current practices, and constructing a translational framework for biomaterial-assisted seroma management. The study has four aims. First, it clarifies the biological and surgical mechanisms that underlie postoperative seroma. Second, it analyzes the strengths and limitations of conventional prevention and treatment approaches. Third, it examines extracellular matrix scaffold science as a biologically plausible intervention paradigm. Fourth, it proposes a clinically meaningful interpretation of how regenerative biomaterials may reshape future surgical strategies for seroma prevention and treatment.

In a field where many surgeons still rely on local habit, individual preference, or reactive escalation, a biologically integrated framework is needed. The references provided make possible such a framework. By bringing together evidence from breast surgery, hernia repair, orthopedic case experience, wound biology, regenerative medicine, and scaffold science, this article argues that postoperative seroma should be understood not merely as a nuisance fluid collection but as a failure of orderly tissue resolution. Preventing

and treating it effectively may therefore require not only drainage and observation, but also strategies that influence how tissue heals, adheres, remodels, and re-establishes function after disruption.

METHODOLOGY

Study Design

This study employed a qualitative integrative research methodology designed to generate an original scholarly synthesis from the provided references. The integrative approach was selected because the source set was heterogeneous in design and purpose. The references included animal experimentation, classification studies, national survey data, case reports, conceptual regenerative medicine analyses, wound-healing studies, and clinically oriented reviews. A conventional quantitative meta-analysis would not have been appropriate because of marked differences in population, intervention, outcome structure, and methodological architecture across the sources. Instead, an integrative qualitative design allowed conceptual aggregation of evidence while preserving contextual specificity.

The use of qualitative integrative analysis in this context is methodologically justified for several reasons. First, seroma research is fragmented across specialties rather than centralized within a single disease-specific evidence model. Second, the role of extracellular matrix biomaterials in seroma management remains translational and emergent; therefore, theoretical synthesis is necessary to connect otherwise isolated findings. Third, several key references are case-based or conceptual rather than comparative trials, which means their value lies not only in isolated outcomes but also in the mechanisms and treatment logic they illuminate. The research objective was therefore not to statistically pool effect sizes, but to develop a coherent explanatory and interpretive model grounded in the provided literature.

Data Source and Corpus

The evidence corpus consisted strictly of the fifteen references supplied by the user. No external sources were introduced, and no supplementary literature was used. This constraint shaped the methodology deliberately. The purpose was to ensure that every interpretive move in the article remained traceable to the designated evidence set.

The reference corpus encompassed the following thematic categories: foundational postoperative seroma overview (Kazzam & Ng, 2023); seroma classification and surgical staging (Morales-Conde, 2012; Petro et al., 2016); real-world surgical practice patterns in breast surgery (Fairhurst et al., 2024);

persistent and delayed seroma case management (Ghazal et al., 2022; Mohamed et al., 2016); prevention of seroma in experimental settings (Agalar et al., 2017); extracellular matrix scaffold biology and host-response theory (Badylak, 2014; Beattie et al., 2009; Turner & Badylak, 2014); and translational or clinical biomaterial use in wound, trauma, and postoperative tissue management (Bettioli et al., 2021; Collins et al., 2023; Diaz-Valadez et al., 2023; Kimmel, 2018; Valerio et al., 2015).

Analytical Procedure

The analytical process unfolded in five stages. In the first stage, each reference was reviewed for primary focus, clinical setting, intervention type, and conceptual contribution. Rather than treating all sources as equivalent, the analysis identified what function each source served within the overall argument. For example, Fairhurst et al. (2024) was treated primarily as evidence of real-world management variation; Badylak (2014) as a mechanistic and theoretical source; Morales-Conde (2012) as a classification-focused clinical framework; and Bettioli et al. (2021) as translational proof-of-concept for scaffold use in postoperative seroma.

In the second stage, recurring thematic patterns were identified across the corpus. Four dominant themes emerged. The first theme was multifactorial pathogenesis, including dead space, disrupted lymphatic channels, inflammatory exudation, motion, and poor tissue adherence. The second theme was variability and insufficiency of conventional management, reflected in survey data, case escalation, and persistent seroma reports. The third theme was constructive tissue remodeling through extracellular matrix scaffolds, including host-response modulation and progenitor-cell recruitment. The fourth theme was translational integration, namely the potential application of biomaterials in seroma prevention and treatment.

In the third stage, cross-context comparison was performed. Here, evidence from different surgical domains was not flattened into one generic conclusion. Instead, the analysis examined how mechanisms repeated across context. For instance, breast surgery and ventral hernia repair differ anatomically, but both involve surgically created planes vulnerable to fluid accumulation and incomplete tissue reattachment. Likewise, chronic wound care and postoperative seroma are distinct clinical states, yet both involve questions of tissue remodeling, inflammatory control, and biologic microenvironment. This stage allowed mechanism-centered rather than procedure-centered interpretation.

In the fourth stage, the evidence was organized into an interpretive progression from problem identification to translational solution. The analytical logic moved from defining seroma as a complex postoperative phenomenon, to recognizing the limits of reactive management, to explaining why extracellular matrix biomaterials may offer biologically coherent alternatives or adjuncts. This progression shaped the Results and Discussion sections.

In the fifth and final stage, the study produced an original conceptual framework that links seroma prevention and treatment to constructive remodeling. This framework does not claim universal clinical proof; rather, it is the principal original contribution of the article. The novelty lies in the synthesis itself: the study connects scaffold biology, wound regeneration, and seroma management into a single explanatory model grounded in the provided literature.

Inclusion Logic and Interpretive Boundaries

All provided references were included in the synthesis. No reference was excluded. However, the analytical weight assigned to each source depended on its evidentiary role. Experimental animal data were interpreted as mechanistic and proof-of-concept evidence rather than direct clinical equivalence. Case reports were used to illustrate clinical possibility, complexity, and treatment rationale, but not generalized as definitive standards of care. Survey data were interpreted as reflective of practice patterns rather than proof of superiority. Theoretical scaffold literature was used to understand host-response and biologic plausibility rather than to overstate procedure-specific efficacy.

This interpretive discipline was crucial because the literature base is supportive but not uniform. For example, it would be methodologically unsound to claim on the basis of one orthopedic case and one animal model that all postoperative seromas should now be treated with porcine-derived scaffolds. Conversely, it would also be intellectually limiting to ignore the translational significance of those studies simply because they are not randomized trials. The methodology therefore balanced openness to emerging innovation with restraint in generalization.

Conceptual Definitions

For the purpose of this study, postoperative seroma was defined as a clinically relevant accumulation of serous fluid within a postoperative space created or maintained by tissue dissection, dead space, lymphatic disruption, inflammatory exudation, or incomplete tissue adherence (Kazzam & Ng, 2023; Morales-Conde, 2012). Complex seroma referred to seromas that are persistent, symptomatic, encapsulated, recurrent,

delayed, infected, or requiring escalated intervention (Ghazal et al., 2022; Mohamed et al., 2016). Extracellular matrix biomaterials referred to decellularized biologic scaffolds derived from allogeneic or xenogeneic tissues intended to support constructive tissue remodeling rather than permanent inert occupation of space (Badylak, 2014; Turner & Badylak, 2014).

Trustworthiness and Rigor

Rigor in qualitative integrative analysis depends on transparency, coherence, and consistency of interpretation. This study sought rigor in four ways. First, the source base was fixed and explicit. Second, all major claims in the article were grounded in one or more supplied references. Third, the argument proceeded through visible thematic logic rather than impressionistic commentary. Fourth, limitations of the evidence base were explicitly acknowledged in the Discussion section.

Although the article is written in the style of a publication-ready research paper, it does not present fabricated patient recruitment, invented statistical datasets, or unreported clinical trials. Its originality lies in comparative synthesis and conceptual advancement. This approach is especially appropriate in an area where translational reasoning is essential to bridge experimental biomaterial science and surgical complication management.

RESULTS

Seroma Emerges as a Multifactorial Failure of Postoperative Tissue Resolution

The first major finding of this analysis is that postoperative seroma cannot be adequately explained by a single mechanism. Across the reference set, seroma repeatedly appears as the result of interacting factors rather than isolated technical error. Kazzam and Ng (2023) frame postoperative seroma management within a broad clinical overview, implicitly recognizing that seroma is common across surgical disciplines and may arise when disrupted tissue planes continue to produce or retain serous fluid. Morales-Conde (2012) reinforces this complexity by proposing classification after laparoscopic ventral hernia repair, indicating that not all seromas share equal biological behavior or clinical significance.

When these sources are read alongside practical surgical studies, five interlocking mechanisms become evident. The first is dead-space persistence. Whenever surgery creates a cavity or broad undermined plane, fluid may accumulate unless tissue planes adhere effectively. The second is lymphatic disruption, especially relevant in procedures involving axillary or

extensive soft-tissue dissection. The third is inflammatory exudation from tissue injury, which may be intensified by thermal damage, foreign material, hematoma residue, or ongoing mechanical irritation. The fourth is shear or movement across tissue surfaces that prevents stable apposition. The fifth is incomplete or dysregulated remodeling, through which the body fails to convert a postoperative cavity into mature, integrated tissue.

This multidimensional interpretation is supported indirectly by the diversity of clinical contexts represented in the references. Seroma occurs after mastectomy and axillary dissection (Agalar et al., 2017; Fairhurst et al., 2024), after ventral and incisional hernia repair (Ghazal et al., 2022; Mohamed et al., 2016; Morales-Conde, 2012; Petro et al., 2016), and even in orthopedic postoperative contexts (Bettioli et al., 2021). Such procedural variation makes it unlikely that one narrow mechanism explains all cases. Rather, seroma appears wherever the conditions for sustained fluid production and incomplete tissue reintegration coexist.

A particularly important interpretive result is that the references collectively shift attention from fluid itself to the postoperative environment that permits fluid persistence. In other words, the fluid collection is not the entire disease state; it is the visible outcome of deeper tissue-organizational failure. This finding becomes crucial when evaluating treatment strategies, because interventions that remove fluid without altering the underlying tissue dynamics may relieve the problem temporarily while leaving the biological basis of recurrence intact.

Current Management Practices Remain Variable, Reactive, and Often Procedure-Specific

The second major finding is that conventional seroma management remains marked by variability and reactive decision-making. Fairhurst et al. (2024), through a national practice survey focused on drains and seroma management after mastectomy and axillary surgery, show that surgeons continue to differ in how they attempt to prevent and manage postoperative fluid collections. This survey-based variability is itself an important result. In conditions where management is strongly standardized, wide practice heterogeneity usually narrows over time. The persistence of heterogeneity here suggests ongoing uncertainty about best practice.

The literature indicates that drains remain a central, though imperfect, component of management. Their logic is intuitive: if postoperative fluid accumulates in dead space, then drainage should reduce both volume and pressure while tissue planes adhere. Yet the very

need for surveys such as that of Fairhurst et al. (2024) suggests that drains do not resolve all questions. Issues remain concerning optimal duration, removal thresholds, patient burden, infection risk, and whether drains merely manage fluid expression without fundamentally promoting biologic resolution.

Reactive methods, especially aspiration and observation, also dominate the clinical landscape described across the references. Kazzam and Ng (2023) present postoperative seroma management in a broad therapeutic spectrum, but the implied treatment ladder remains largely reactive: monitor, aspirate, compress, drain, and escalate when persistent. Ghazal et al. (2022) illustrate what happens when this ladder becomes insufficient. Their case of persistent complex seroma required capsulectomy and scarification using argon beam coagulator, demonstrating that long-standing seromas may develop structural pathology beyond simple free fluid accumulation. Once a fibrous cavity or persistent secretory surface is established, routine aspiration may become repetitive rather than curative.

Mohamed et al. (2016) provide another revealing insight. Delayed onset seroma five years after ventral incisional hernia repair suggests that the timeline of seroma cannot always be reduced to immediate postoperative wound drainage. The result is conceptually significant because it points to the possibility that tissue interfaces, implanted materials, or remodeling processes may remain vulnerable to fluid reaccumulation even long after presumed healing. A management philosophy focused only on early drains and aspirations does not fully address such chronicity or delayed presentation.

The analysis also finds that classification matters because it structures treatment reasoning. Morales-Conde (2012) proposed a classification for seroma after laparoscopic ventral hernia repair, thereby moving the field away from undifferentiated terminology. Classification systems do more than name problems; they shape thresholds for action. A small asymptomatic collection and a persistent symptomatic encapsulated seroma should not be managed as identical phenomena. Petro et al. (2016), though centered on ventral hernia staging, contribute to this broader finding by showing that complication reasoning benefits from structured categorization. One of the results of the present analysis is therefore that seroma management improves conceptually when surgeons distinguish severity, duration, symptom burden, and tissue context rather than treating all postoperative fluid collections as clinically equivalent.

Persistent and Complex Seroma Represents a Distinct

Clinical Problem

A third major finding is that persistent or complex seroma should be treated as a distinct subtype rather than merely a longer-lasting version of ordinary postoperative fluid collection. Ghazal et al. (2022) and Mohamed et al. (2016) are especially important in establishing this point. In persistent complex seroma, the problem is not only that fluid remains present. Rather, the cavity itself may become biologically active, fibrotic, recurrent, or resistant to ordinary treatment. Delayed onset seroma similarly implies that the postoperative space may retain pathophysiologic potential over time.

This finding leads to two interpretive consequences. First, chronic seroma is not fully explained by incomplete drainage. Second, management of persistent seroma may require transformation of the tissue bed, not just evacuation of accumulated fluid. The success of capsulectomy and scarification in the case reported by Ghazal et al. (2022) reflects this principle: treatment acted upon the tissue architecture of the seroma cavity, not merely the fluid within it.

The consequence for surgical thinking is substantial. Once persistent seroma is understood as a problem of pathologic cavity persistence, therapies that encourage constructive tissue integration become theoretically attractive. This is where the literature on extracellular matrix biomaterials becomes especially relevant.

Extracellular Matrix Scaffolds Function Through Biologic Signaling and Constructive Remodeling Rather Than Passive Occupation

The fourth major finding is that extracellular matrix scaffolds should not be interpreted merely as biologic fillers. The references on scaffold biology consistently emphasize that these materials function through dynamic host interaction. Badylak (2014) argues that decellularized allogeneic and xenogeneic tissues act as bioscaffolds whose clinical performance depends on factors influencing host response. This shifts the interpretive frame away from the simplistic idea that biologic materials are valuable only because they occupy space. Instead, they may alter the microenvironment in which healing occurs.

Beattie et al. (2009) provide particularly important mechanistic evidence by demonstrating chemoattraction of progenitor cells by remodeling extracellular matrix scaffolds. The significance of this result extends beyond wound repair into postoperative seroma theory. If scaffold materials recruit progenitor cells and influence regenerative cascades, then they may help convert unstable postoperative spaces into remodeling tissue beds more effectively than passive drainage alone.

Turner and Badylak (2014) further support this interpretation through discussion of biologic scaffolds in chronic nonhealing wounds. Chronic wounds are not identical to seromas, but the healing principles overlap. Both involve abnormal persistence of a postoperative or post-injury state, both can be characterized by dysregulated microenvironments, and both may benefit from interventions that guide tissue remodeling rather than merely cover defects. A key result of the present synthesis is therefore that extracellular matrix scaffolds are conceptually relevant to seroma because seroma is, at least in part, a disorder of failed or delayed constructive remodeling.

Preclinical and Translational Evidence Supports a Rationale for Biomaterial-Assisted Seroma Prevention

A fifth major finding is that the available evidence, although limited and heterogeneous, supports a plausible role for biomaterials in seroma prevention and treatment. Agalar et al. (2017) demonstrated that porcine dermal collagen prevented seroma formation after mastectomy and axillary dissection in rats. This is highly relevant because it directly links a biomaterial intervention to seroma prevention in a model involving tissue planes and lymphatic disruption similar to clinically important breast procedures.

Animal data should not be overgeneralized, but their mechanistic value is substantial. In the context of the present synthesis, the rat study suggests that biomaterial application may reduce the conditions that allow seroma to form, possibly by supporting adherence, modulating inflammation, or improving the quality of tissue repair. Even if the precise mechanism remains incompletely defined within the source itself, the finding aligns closely with scaffold biology theory from Badylak (2014) and Beattie et al. (2009).

Clinical translational support is also present. Bettiol et al. (2021) described the use of a porcine bladder extracellular matrix scaffold to treat postoperative seroma in a total knee arthroplasty patient. As a case report, this does not prove population-level efficacy. However, its value lies in demonstrating real-world application of the concept. It shows that surgeons have already begun using extracellular matrix materials not just for broad wound reconstruction but specifically for postoperative seroma management.

Further translational support appears in wound and soft-tissue management literature. Valerio et al. (2015) discussed the use of urinary bladder matrix in trauma and combat casualty wound care, emphasizing tissue restoration within difficult wound environments. Collins et al. (2023) described management of crush injury with significant soft tissue loss using biological and dynamic tissue systems. Diaz-Valadez et al. (2023)

reported clinical and histologic wound-healing responses with multi-tissue extracellular matrix, including cost analysis compared with negative pressure wound therapy. Kimmel (2018) highlighted biomaterial powder focused on cell signaling in wound healing applications. These studies are not seroma trials, yet they converge on the principle that biologic materials can influence the trajectory of healing in complex tissue settings.

The result, then, is not that scaffold therapy is already proven as standard seroma care, but that the biologic rationale for such therapy is unusually coherent across basic science, preclinical prevention, and selected clinical applications. That coherence is one of the strongest outcomes of this integrative analysis.

Biomaterial Use Suggests a Shift from Fluid Evacuation to Tissue Reorganization

A sixth result of the study is conceptual rather than procedural. Across the reference set, biomaterial-assisted treatment implies a different therapeutic philosophy. Conventional seroma management generally seeks to control what has accumulated. Biomaterial-based thinking seeks to change why accumulation persists.

This distinction is subtle but foundational. Drains, aspiration, compression, and even some operative revisions primarily target the fluid burden or the cavity after it becomes problematic. Extracellular matrix biomaterials, in contrast, aim to affect tissue behavior at the interface of healing. By altering inflammatory signaling, facilitating host cell migration, supporting constructive remodeling, and potentially reducing shear-prone dead space, such materials may interrupt the biological cycle that sustains seroma.

This does not mean traditional measures become obsolete. Instead, the result of the present analysis is that seroma care may be most effective when mechanical and biologic strategies are integrated. For example, drainage may still be useful in the immediate postoperative period, but long-term resolution may depend on whether tissue planes achieve biologically sound reintegration. The references collectively support movement toward such a combined model.

Evidence Strength Is Promising but Not Definitive

The seventh major finding concerns the quality and limitations of the available evidence. The literature is encouraging, but it is not yet definitive. Strong mechanistic and conceptual support exists for extracellular matrix biomaterials, especially through Badylak (2014), Beattie et al. (2009), and Turner and Badylak (2014). Supportive direct or indirect clinical evidence exists through Agalar et al. (2017), Bettiol et

al. (2021), Diaz-Valadez et al. (2023), and other wound-healing studies. Yet the evidence base lacks large standardized comparative trials focused specifically on postoperative seroma across procedure types.

This mixed evidentiary profile is itself an important result. It explains why practice remains variable and why the field has not fully embraced biologic scaffolds as routine care. At present, the literature supports plausibility, selected success, and conceptual integration more strongly than universal protocolization.

DISCUSSION

The findings of this study suggest that postoperative seroma should be reinterpreted through a broader biologic and surgical lens than is commonly applied in routine care. The conventional description of seroma as a simple fluid collection is inadequate because it reduces a multifactorial postoperative event to its most visible symptom. The reference set examined in this study instead supports a model in which seroma is a disorder of postoperative space, inflammatory persistence, disrupted lymphatic drainage, incomplete tissue adherence, and delayed or dysregulated remodeling (Kazzam & Ng, 2023; Morales-Conde, 2012). This expanded understanding has profound implications for how clinicians classify, prevent, and treat the condition.

One of the most important interpretive insights emerging from this analysis is that seroma belongs at the intersection of surgical mechanics and regenerative biology. In traditional surgical reasoning, seroma is often managed as a residual technical problem: a drain-related issue, a dead-space issue, or a follow-up nuisance. While none of these descriptions is entirely wrong, each is incomplete. They emphasize the external management of postoperative consequences rather than the internal biology of postoperative repair. Once the literature on extracellular matrix scaffolds is brought into conversation with the seroma literature, however, a more ambitious model becomes possible. In this model, effective seroma control depends not only on removing fluid and closing cavities but on directing the wound environment toward constructive healing.

This shift matters because many of the limitations of conventional care stem from its fundamentally reactive structure. Drains are placed because fluid is expected. Aspirations are performed because fluid has accumulated. Compression is applied because tissues have not adhered adequately. Reoperation is considered because chronicity has emerged. Even when these measures succeed, they often do so by managing manifestations rather than transforming the

wound biology that generated them. The practice variability observed by Fairhurst et al. (2024) is therefore unsurprising. If the field lacks a strongly validated biologic model of resolution, then surgeons will continue to rely on institutional norms, personal experience, and procedure-specific habit.

This analysis does not argue that conventional approaches are unhelpful. On the contrary, drainage, observation, aspiration, and careful follow-up remain important, and in many cases they may be sufficient (Kazzam & Ng, 2023). Yet the evidence of persistent complex seroma and delayed onset seroma demonstrates that such approaches are not universally curative (Ghazal et al., 2022; Mohamed et al., 2016). In chronic cases, the problem evolves beyond transient fluid retention. The tissue cavity itself may become pathologically maintained. Fibrous capsule formation, chronic exudative behavior, local motion, and failed tissue integration may create a self-perpetuating microenvironment in which aspirations temporarily empty the space but do not abolish the biologic conditions of recurrence.

This observation is central to understanding why extracellular matrix biomaterials may matter. Their relevance is not that they are biologic in a vague or fashionable sense. Their relevance lies in the specific way they engage healing. Badylak (2014) emphasized that the performance of decellularized biologic scaffolds depends on host response. That proposition is critical because it locates scaffold effectiveness not in mere presence but in biologic interaction. The scaffold is not simply a patch, a plug, or a neutral dressing. It is a signaling and remodeling environment. When paired with Beattie et al. (2009), who demonstrated progenitor-cell chemoattraction by remodeling extracellular matrix scaffolds, the implication becomes even stronger: such materials may help recruit the very cellular processes needed to convert unstable postoperative planes into mature, integrated tissue.

In theoretical terms, seroma prevention and treatment can therefore be understood as a problem of tissue destiny. After surgical dissection, the body must decide whether a newly created space becomes obliterated through organized healing or remains available for recurrent fluid accumulation. Conventional mechanical approaches influence this decision indirectly. Biologic scaffolds may influence it more directly by providing structural cues, modulating inflammation, and inviting constructive cellular occupation of the space. This does not mean all extracellular matrix materials will perform identically or that all seroma-prone sites will respond the same way. It means that scaffold use is theoretically aligned with the deeper biology of the problem.

The animal study by Agalar et al. (2017) is especially important in this regard because it directly links porcine dermal collagen to prevention of seroma formation after mastectomy and axillary dissection. The breast and axillary context is clinically significant. These are regions where lymphatic disruption, large undermined planes, and motion can combine to produce frequent postoperative seroma. A biomaterial that reduces seroma in such a model may be influencing more than mechanical closure; it may be facilitating a different quality of tissue response. Even though animal models cannot be transferred wholesale into human guidelines, their conceptual contribution is substantial. They show that seroma prevention is not limited to drain strategy and operative technique. Biomaterial-mediated modulation is biologically plausible.

The translational relevance of this idea becomes more compelling when clinical reports are considered. Bettiol et al. (2021) described successful use of porcine bladder extracellular matrix scaffold for postoperative seroma in a total knee arthroplasty patient. That report matters because it expands the discussion beyond abdominal wall or breast surgery and suggests that the core issue may be common to postoperative spaces in multiple anatomical regions. Likewise, wound-healing and trauma literature demonstrates that extracellular matrix materials are capable of supporting repair in environments far more hostile than typical postoperative seroma cavities (Valerio et al., 2015; Collins et al., 2023; Turner & Badylak, 2014). If such materials can assist healing in trauma, chronic wounds, or tissue loss, then their application in seroma-prone surgery deserves serious consideration rather than being regarded as experimental novelty alone.

The broader wound-healing literature within the provided references also enriches the discussion in another way: it reminds us that healing is not simply closure. Healing includes signaling, recruitment, matrix turnover, angiogenic support, immune orchestration, and eventual tissue remodeling. Kimmel (2018) emphasized biomaterial powder focused on cell signaling, while Diaz-Valadez et al. (2023) described clinical and histologic wound-healing responses with multi-tissue extracellular matrix. These sources collectively suggest that the future of postoperative complication management may depend on interventions that influence local biologic communication. Seroma can thus be interpreted not only as a mechanical cavity filled with fluid, but as a local failure of instructive healing signals sufficient to achieve stable resolution.

A reasonable counterargument must nevertheless be considered. One could argue that the scaffold literature cited here is overly broad and that evidence from

chronic wounds, trauma, or tissue loss may not translate directly to seroma. This objection is valid and should be taken seriously. A chronic nonhealing wound is not the same as a postoperative seroma, and wound-healing success does not automatically imply seroma prevention. However, the relevance of these studies lies in shared healing principles rather than identical indications. The common denominator is the challenge of converting a disrupted tissue environment into a stable and integrated repair. Seroma is one manifestation of failure in that conversion. Thus, while direct evidence remains limited, the theoretical transfer is neither arbitrary nor weak. It is grounded in mechanistic overlap.

Another counterargument is economic and logistical. Biomaterials may be more expensive than standard drains, compressive dressings, or serial aspiration, and not all institutions can incorporate them easily into routine practice. Diaz-Valadez et al. (2023) are therefore particularly important because they include cost analysis compared with negative pressure wound therapy. Although the study context is wound healing rather than postoperative seroma alone, it raises the crucial issue that cost must be evaluated not simply by acquisition price but by total episode-of-care value. Repeated aspirations, additional clinic visits, delayed recovery, infection risk, prolonged wound care, and reoperation all carry costs. A biomaterial that appears expensive up front may become justifiable if it reduces chronicity, intervention frequency, or downstream complications. At the same time, such economic arguments require stronger seroma-specific outcome studies before broad implementation can be advocated confidently.

The present analysis also highlights the importance of classification and staging in future progress. Morales-Conde (2012) made an essential contribution by proposing a classification system for seroma after laparoscopic ventral hernia repair. In surgical complications, classification is not merely descriptive. It determines whether clinicians can compare cases meaningfully, stratify severity, and design targeted research. One of the reasons seroma management remains diffuse may be that many studies and clinical records do not distinguish adequately between expected asymptomatic fluid collections, clinically relevant symptomatic seromas, persistent recurrent cavities, delayed late seromas, and complex encapsulated lesions. The field needs more than the generic label "seroma." It needs clinically useful subtypes linked to management pathways. Petro et al. (2016), through their work on ventral hernia staging, reinforce the value of structured risk and complication frameworks. Future biomaterial studies in seroma

would be considerably more interpretable if they were designed around standardized seroma categories.

The implications for breast surgery are especially noteworthy. Fairhurst et al. (2024) demonstrate that management practices remain varied after mastectomy and axillary surgery, suggesting persistent uncertainty despite decades of clinical experience. This is an important reminder that common complications do not necessarily become simple over time. The more frequently surgeons encounter a complication without definitive resolution, the more likely it is that the underlying biology has been underestimated. In breast surgery, where lymphatic disruption and large flaps are common, a biologically informed prevention strategy may be particularly valuable. The finding from Agalar et al. (2017) that porcine dermal collagen prevented seroma formation in a mastectomy and axillary model is therefore more than a niche experimental observation. It may signal a future direction for procedure-specific innovation.

The ventral hernia literature introduces additional nuance. Ventral hernia repair often involves prosthetic materials, broad dissection, component separation, and altered tissue mechanics. Seroma in this setting may therefore reflect not only dead space and exudation but also long-term interface behavior between tissue and implanted material. The delayed onset case reported by Mohamed et al. (2016) is especially provocative because it raises the possibility that postoperative planes may remain biologically unsettled for years. This should caution against overly narrow postoperative surveillance models and encourage longer-term thinking about tissue integration. If future biomaterial approaches are adopted in abdominal wall surgery, they will need to be studied not only for early drainage reduction but also for long-term remodeling outcomes.

From a regenerative surgery perspective, the most promising conceptual contribution of this article is the proposal that seroma management should transition from evacuation-centered care to resolution-centered care. Evacuation-centered care asks how best to remove fluid. Resolution-centered care asks how best to restore the tissue environment so that fluid no longer accumulates pathologically. The difference between these two orientations may shape the next generation of research. In evacuation-centered paradigms, trial endpoints might include drain duration or aspiration frequency. In resolution-centered paradigms, endpoints would also include time to durable tissue adherence, recurrence prevention, histologic remodeling quality, patient burden, and total treatment episode.

This shift also has educational consequences. Surgeons are often trained to manage seroma pragmatically, which is understandable. Yet practical management without a robust conceptual model can lead to repetitive low-level interventions that fail to advance the field. Integrating scaffold biology and regenerative principles into surgical education may help clinicians distinguish when a seroma is likely to resolve with routine measures and when it represents an opportunity for biologically targeted intervention. Such education would also encourage greater collaboration between surgeons, wound-healing specialists, reconstructive experts, and biomaterials researchers.

Despite the promise identified in this analysis, several limitations must be acknowledged. The first limitation is the heterogeneity of the evidence base. The included references differ in design, specialty, sample structure, and evidentiary strength. National survey data, animal studies, case reports, and conceptual reviews cannot be treated as equivalent forms of evidence. The second limitation is that direct seroma-specific biomaterial trials are limited within the provided corpus. The argument for extracellular matrix use is therefore stronger in biologic plausibility and translational coherence than in definitive comparative proof. The third limitation is that not all provided references report standardized outcome measures. This makes cross-study comparison difficult and reinforces the need for future reporting frameworks. The fourth limitation is that the analysis was intentionally restricted to the supplied references and therefore did not incorporate broader external literature that may support, refine, or challenge some conclusions.

These limitations, however, do not weaken the main contribution of the study. They clarify its function. This article is an original integrative analysis that identifies a neglected conceptual bridge in the literature. It does not claim to close the empirical question; it defines the question more precisely. That alone is valuable in a field where clinical habits often outpace theoretical integration.

Future research should proceed in several directions. First, seroma studies should adopt consistent classification systems so that prevention and treatment outcomes can be compared meaningfully across procedures. Second, prospective clinical studies should evaluate extracellular matrix biomaterials not only as salvage tools for persistent seroma but also as prophylactic adjuncts in high-risk operations. Such studies should distinguish between anatomical sites, because breast, abdominal wall, and orthopedic tissues may differ in biologic response and cost-benefit profile. Third, histologic and imaging-based studies should examine how biomaterials affect tissue adherence,

lymphatic remodeling, inflammatory persistence, and cavity obliteration over time. Fourth, health-economic analyses should compare biologic scaffold use against repeated aspiration, prolonged drainage, negative pressure systems, and reoperation. Fifth, long-term follow-up is essential, particularly in light of delayed seroma phenomena described by Mohamed et al. (2016).

The future clinical role of extracellular matrix biomaterials in seroma management will likely not be universal or one-size-fits-all. It may instead emerge in stratified indications: high-risk mastectomy planes, recurrent abdominal wall seromas, chronic encapsulated cavities, or postoperative spaces where mechanical measures repeatedly fail. Such selective adoption would be consistent with the current evidence. Even if biomaterials do not replace drains or aspirations entirely, they may transform outcomes in precisely those cases where conventional care reaches its limit.

Ultimately, the present study suggests that postoperative seroma should be regarded as a model complication for the broader evolution of surgery itself. Surgery is moving from purely technical correction toward biologically informed reconstruction. As that transition continues, complications like seroma cannot remain conceptualized only in terms of fluid volume and drain output. They must be understood in terms of tissue ecology, host response, and guided remodeling. The references analyzed here strongly support that transformation.

CONCLUSION

Postoperative seroma remains a significant and under-theorized complication across modern surgical practice. The evidence synthesized in this article shows that seroma is not merely a passive fluid collection but a multifactorial postoperative disorder rooted in dead-space persistence, lymphatic disruption, inflammatory exudation, mechanical instability, and incomplete tissue remodeling (Kazzam & Ng, 2023; Morales-Conde, 2012). Conventional strategies such as drains, aspiration, compression, and observation remain important, but the literature also reveals their limitations, particularly in persistent, complex, or delayed seroma cases (Fairhurst et al., 2024; Ghazal et al., 2022; Mohamed et al., 2016).

A central contribution of this analysis is the integration of regenerative biomaterial science with seroma management. Extracellular matrix-based biologic scaffolds emerge from the provided references not as passive fillers but as active modulators of host response, progenitor-cell recruitment, and constructive remodeling (Badylak, 2014; Beattie et al.,

2009; Turner & Badylak, 2014). Experimental prevention data, translational case reports, and wound-healing applications collectively suggest that biomaterials may reduce seroma burden by changing the biology of postoperative spaces rather than merely treating the fluid they produce (Agalar et al., 2017; Bettiol et al., 2021; Diaz-Valadez et al., 2023; Valerio et al., 2015).

The field is not yet supported by sufficient large-scale seroma-specific comparative trials to justify universal protocol adoption. Nevertheless, the current evidence justifies a clear conceptual shift. Seroma management should evolve from an evacuation-centered model toward a resolution-centered model that emphasizes tissue reintegration, inflammatory regulation, and durable cavity obliteration. Future research should therefore prioritize standardized classification, prospective biomaterial evaluation, histologic outcome assessment, and health-economic comparison across procedure types.

In summary, the literature provided supports a compelling thesis: the next meaningful advance in postoperative seroma care is unlikely to come from more refined fluid removal alone. It is more likely to arise from biologically informed strategies that help tissue heal in a more organized, adhesive, and regenerative manner. Extracellular matrix biomaterials represent one of the most promising frameworks for achieving that transition.

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