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Application of Cryopreserved Cord Blood Preparations in Combined Treatment of Diabetes Mellitus Complications

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Abstract

The article examines cryopreserved cord blood preparations as adjunctive agents in combined treatment of diabetes mellitus complications, with attention to diabetic foot syndrome, chronic ulcers, infected soft-tissue lesions, and delayed wound repair. The relevance of the topic derives from the limited ability of standard surgical, antimicrobial, vascular, and metabolic correction to restore reparative capacity in diabetic tissues after infection control and debridement. The study aims to systematize recent evidence on cord blood-derived cellular, humoral, and vesicular products and connect it with earlier cryomedical surgical experience. Source analysis, comparative synthesis, typological classification, and analytical generalization formed the methodological base. The material corpus contains sixteen scientific sources, including recent clinical studies, systematic reviews, experimental studies, and earlier cryomedical publications on Cryocord-C and combined surgical treatment of purulent-necrotic diabetic foot lesions. The analytical section identifies three therapeutic vectors: immune recalibration, repair stimulation, and metabolic-homeostatic support. Practical value lies in a staged implementation model that links cord blood-derived preparations with wound readiness, safety control, and measurable clinical response.

Keywords: Cryopreserved cord blood, Diabetes complications, Platelet lysate, Healing, and Immunomodulation.

1. Introduction

Late complications of diabetes mellitus develop through the interaction of chronic hyperglycemia, endothelial dysfunction, oxidative stress, impaired immune response, and reduced tissue regeneration. In diabetic foot syndrome, these disturbances are combined with peripheral neuropathy, ischemia, infection, altered proteolysis, and defective extracellular matrix

remodeling. Persistent macrophage activation, insufficient transition to a reparative phenotype, reduced angiogenesis, and impaired collagen deposition prevent the wound from progressing from inflammation to granulation and epithelialization (Teng *et al.*, 2022; Yan *et al.*, 2022; Habib, 2022; Yang *et al.*, 2024). Standard treatment comprises debridement, drainage, antimicrobial therapy, revascularization

when indicated, glycemic control, offloading, and appropriate wound dressings. Despite adequate removal of necrotic tissue and suppression of acute infection, some diabetic wounds retain persistent inflammation and low reparative activity.

Current guidelines consider biological and regenerative interventions as adjuncts to multidisciplinary diabetic foot care rather than substitutes for surgical debridement, infection control, vascular assessment, offloading, and metabolic stabilization (Chen *et al.*, 2024). Their clinical use is therefore justified only after the principal mechanical, infectious, and ischemic barriers to wound healing have been controlled. Cryopreserved cord blood preparations can be considered biological adjuncts at the stage when conventional treatment has controlled necrosis, infection, pressure overload, and critical perfusion disorders, but the wound still demonstrates weak granulation and delayed epithelialization. The therapeutic rationale concerns the delivery of soluble and cellular signals capable of reducing excessive inflammation, supporting angiogenesis, stimulating fibroblast and endothelial activity, and improving extracellular matrix remodeling. Earlier cryomedical work on Cryocord-C and related preparations placed these products inside combined surgical treatment of purulent complications of type 2 diabetes. The earliest clinical reports on Cryocord-C described its use in diabetic foot syndrome and purulent-necrotic diabetic lesions as part of a combined surgical strategy rather than as an isolated regenerative intervention (Popovych, 2005a, 2005b, 2006). A current academic review needs to move beyond repetition of that clinical line and interpret it through recent evidence on cord blood serum, platelet lysate, mesenchymal stem cell derivatives, mononuclear cells, exosomes, and secretome-based regenerative therapy.

Recent studies provide clinical support for several cord blood-derived therapeutic formats. Topical umbilical cord blood platelet lysate gel was associated with greater reduction of diabetic foot ulcer area and more frequent wound closure than saline dressing used within standard care (Lambadiari *et al.*, 2024). Combined application of umbilical cord blood serum and amniotic membrane has been investigated as a

method of joining soluble trophic mediators with structural support for diabetic wound regeneration (Montague *et al.*, 2024). Higher-level evidence on stem cell therapy indicates improvement in wound healing, ulcer size, perfusion-related indicators, and amputation outcomes, although results vary according to cell source, treatment protocol, and study design (Shi *et al.*, 2024; Shannoon, 2025; Tong *et al.*, 2025).

The available literature does not clearly distinguish between living-cell preparations, cord blood serum, platelet lysates, secretomes, and extracellular vesicles. These products differ in biological composition, manufacturing requirements, mechanisms of action, safety profile, and level of clinical evidence. Findings obtained for one therapeutic format therefore cannot be transferred directly to another. A separate analytical problem concerns the stage of combined treatment at which cryopreserved cord blood preparations may be used and the clinical indicators suitable for evaluating response. The aim of this article is to develop an analytical model for the use of cryopreserved cord blood preparations in combined treatment of diabetes mellitus complications, with emphasis on immunomodulatory, reparative, and metabolic mechanisms.

The first research objective is to define how recent evidence explains the biological effects of cord blood-derived preparations in diabetic tissue injury. The second objective is to compare cellular, humoral, and cell-free therapeutic formats in relation to diabetic foot syndrome and chronic diabetic wounds. The third objective is to formulate clinical implementation logic for integrating cryopreserved cord blood preparations into combined treatment without overstating the current evidence base. The novelty of the article lies in the differentiated interpretation of cryopreserved cord blood preparations as components of staged biological support after surgical sanitation, infection control, vascular assessment, and metabolic stabilization. The proposed approach distinguishes cryopreserved serum preparations from living-cell, platelet lysate, and extracellular vesicle therapies and defines their potential clinical placement according to wound readiness and measurable treatment response. The hypothesis states that cryopreserved cord blood preparations have the strongest rationale in diabetes

complications when clinicians use them as adjunctive regulators of the post-sanitation wound environment, with expected effects concentrated in immune balance, repair activation, and metabolic-homeostatic correction.

2. Materials and Methods

The material base was formed through a targeted search in PubMed, PubMed Central, Frontiers, SpringerLink, ScienceDirect, MDPI, and journal platforms covering cryobiology, regenerative medicine, diabetes complications, wound repair, and cell-derived therapies. The search combined the terms “cryopreserved cord blood,” “umbilical cord blood serum,” “diabetic foot,” “diabetic wound,” “platelet lysate,” “mesenchymal stem cell-derived exosomes,” “cord blood Treg exosomes,” “stem cell therapy diabetic foot,” and “diabetes complications.” The initial pool contained 64 records. Screening excluded publications without a direct connection to diabetes complications, studies limited to unrelated wound models, papers centered only on general stem cell biology, duplicates, and publications with unclear journal status. Sixteen scientific sources remained in the final corpus. The selected material included earlier cryomedical clinical publications on Cryocord-C and cord blood preparations in diabetic foot syndrome, purulent-necrotic lesions, and combined surgical treatment of diabetes-related complications (Popovych, 2005a, 2005b, 2006, 2014a, 2014b), one peer-reviewed clinical article on cryopreserved cord blood preparations in purulent complications of type 2 diabetes (Popovych, 2014c), recent clinical evidence on umbilical cord blood platelet lysate and combined cord blood serum application in diabetic wounds (Lambadiari *et al.*, 2024; Montague *et al.*, 2024), systematic and umbrella reviews of stem cell therapy in diabetic foot (Shi *et al.*, 2024; Sun *et al.*, 2022; Tong *et al.*, 2025), a review of human umbilical cord blood therapy for diabetes mellitus (Chaudhari *et al.*, 2022), and experimental studies on exosomes derived from human umbilical cord mesenchymal stem cells or cord blood regulatory T cells (Teng *et al.*, 2022; Yan *et al.*, 2022; Yang *et al.*, 2024). The literature map covered four groups of questions: clinical adjunctive use, cellular therapy outcomes, humoral cord blood products, and cell-free paracrine mechanisms.

The study used source analysis to extract clinically relevant claims, comparative analysis to differentiate cord blood-derived therapeutic formats, conceptual synthesis to connect cryopreservation, surgery, immunomodulation, and wound repair, typological classification to separate cellular, humoral, and extracellular vesicle-based mechanisms, and analytical generalization to build an implementation model aligned with the research objectives.

3. Results

The selected literature supports a restrained but biologically coherent interpretation of cryopreserved cord blood preparations in diabetes complications. Earlier clinical cryomedical work described combined surgical treatment in patients with type 2 diabetes complications, including diabetic foot syndrome, pyonecrotic stages, and purulent lesions, where clinicians added Cryocord-C or related cord blood preparations to operative and pharmacological care (Popovych, 2005a, 2005b, 2006, 2014a, 2014b, 2014c). Reported effects concerned faster wound cleansing, restriction of the pyo-inflammatory process, disappearance of lower-leg edema, improvement in reparative processes, and correction of metabolic-homeostatic disturbances (Popovych, 2005a, 2005b, 2006, 2014a, 2014b, 2014c). The clinical value of this source lies in its treatment logic. The preparation was placed after surgical sanitation and inside a broader therapeutic complex. That placement still offers the safest academic position for regenerative adjuncts in diabetic foot syndrome.

Recent studies give this older surgical logic a more detailed biological language. Researchers have assessed stem cell therapy for diabetic foot in several systematic reviews and meta-analyses. One meta-analysis update reported better outcomes for stem cell therapy than for conventional methods in wound healing, lower extremity ischemia indicators, pain-free walking distance, rest pain, and amputation-related outcomes (Sun *et al.*, 2022). An umbrella review connected benefit with healing rate, amputation rate, ankle-brachial index, transcutaneous oxygen pressure, ulcer size reduction, healing time, pain-free walking distance, rest pain score, and angiogenesis rate (Shi *et al.*, 2024). These findings do not prove equal efficacy

for every cord blood-derived product. They support a narrower point: clinicians can influence diabetic foot progression when biological therapy addresses vascular and reparative deficits that antibiotics, dressings, and debridement do not fully correct.

Comparison of several sources refines this point. Sun *et al.* (2022) focus on pooled clinical outcome indicators. Shi *et al.* (2024) assess the credibility of systematic reviews and meta-analyses, shifting attention from isolated positive results to the stability of higher-level evidence. Tong *et al.* (2025) compare stem cells from different sources and report improvement in wound healing across sources, with variation in effect size and heterogeneity. The cryomedical publications by Popovych give a narrower surgical setting, where Cryocord-C, cord blood-derived preparations, operative sanitation, anesthesiological support, and local management of purulent-necrotic diabetic lesions are considered within one combined treatment trajectory (Popovych, 2005a, 2005b, 2006, 2014a, 2014b, 2014c). These four positions support one clinical inference: cryopreserved cord blood preparations have the strongest rationale as staged biological support after surgeons have converted an infected lesion into a wound capable of repair.

Cord blood-derived preparations differ in composition and expected action. Human umbilical cord blood contains cellular populations, soluble mediators, growth factors, cytokines, and immunoregulatory elements. A review of human umbilical cord blood therapy for diabetes mellitus notes low potential for graft-versus-host disease and tumorigenicity, lack of routine immunosuppression in discussed settings, and experimental evidence for effects on glycemia, nephropathy, neuropathy, and beta-cell related mechanisms (Chaudhari *et al.*, 2022). This source broadens the discussion beyond wound closure. Diabetes complications remain systemic, even when clinicians see a local ulcer or purulent focus. A cord blood-derived preparation therefore needs evaluation through local wound repair and through the metabolic-inflammatory background that shapes repair. Clinical evidence on umbilical cord blood platelet lysate makes the humoral component more concrete. In diabetic foot

ulcer treatment, topical umbilical cord blood platelet lysate gel was associated with greater ulcer size reduction than regular saline dressing, with a higher proportion of patients showing decreased ulcer area by the end of follow-up (Lambadiari *et al.*, 2024). This result matters because platelet lysate shifts attention from transplantation of living cells to concentrated biological mediators. That format stands closer to cryopreserved serum or extract preparations, where the therapeutic reasoning centers on soluble growth factors, immunoregulatory proteins, and trophic signals.

Another clinical tissue-product model combines umbilical cord blood serum with amniotic membrane. The published rationale links umbilical cord blood serum with growth factors and chemokines, while the amniotic membrane supplies scaffold-like support for tissue repair. The study described possible promotion of diabetic wound regeneration and noted infection-related risks in cellular tissue product therapy, along with non-healing patterns linked to slough formation (Montague *et al.*, 2024). This evidence sharpens the conditions for application. Cord blood serum can support regeneration only when the wound bed has been prepared, monitored, and protected from persistent contamination. In infected diabetic foot lesions, the preparatory surgical stage carries direct biological meaning. It creates the conditions in which a preparation can support repair instead of being consumed by ongoing necrotic inflammation.

Experimental exosome studies clarify the immunomodulatory mechanism. Exosomes derived from human umbilical cord mesenchymal stem cells supported diabetic wound repair through anti-inflammatory macrophage induction, angiogenesis, and collagen remodeling (Teng *et al.*, 2022). Another study reported that human umbilical cord mesenchymal stem cell-derived exosomes accelerated diabetic cutaneous wound healing through reduction of oxidative stress and promotion of angiogenesis (Yan *et al.*, 2022). These findings do not serve as direct clinical proof for cryopreserved cord blood serum. Their value lies in the paracrine logic. They support the idea that many regenerative effects attributed to cell-based therapy are mediated through secreted

vesicles, proteins, microRNAs, and immunological signals. Cryopreserved cord blood preparations can therefore be placed in a broader family of paracrine and humoral biological therapies. Cord blood regulatory T cell-derived exosomes add an immune-specific layer. Researchers reported enhanced endothelial and fibroblast migration, accelerated diabetic wound healing, reduced inflammatory factors, and increased M2 macrophage ratio in vivo (Yang *et al.*, 2024). This evidence is relevant to the first objective because diabetic wounds often remain trapped in an inflammatory phase. Excessive neutro-

phil activity, impaired macrophage transition, and delayed extracellular matrix organization form a persistent injury loop. A cord blood-derived preparation with immunomodulatory activity has clinical value when clinicians understand it as a tool for recalibrating the wound environment, not as a stimulant of tissue growth alone. Figure 1 presents the proposed mechanistic sequence. The scheme reflects the convergence between surgical sanitation, cord blood-derived mediators, inflammatory control, angiogenic support, matrix remodeling, and wound closure.

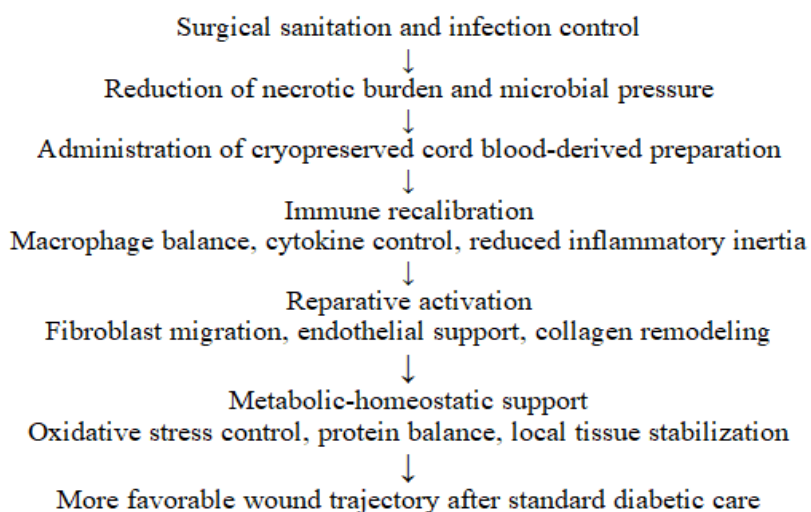


Fig. 1: Mechanistic pathway of cryopreserved cord blood preparations in combined treatment of diabetic complications (compiled by the author based on Popovych, 2014; Teng *et al.*, 2022; Yan *et al.*, 2022; Yang *et al.*, 2024).

The second objective requires comparison of therapeutic formats. Cellular therapies provide a broad biological repertoire, but clinicians and regulators face questions of viability, dose standardization, immune compatibility, production control, and safety surveillance. Humoral preparations, including serum and platelet lysate, fit a mediator-based model with greater clarity. Their expected action centers on growth factors, cytokines, chemokines, and protein regulators. Extracellular vesicle-based approaches isolate part of the paracrine signaling system, but manufacturing standards and clinical dosing still remain difficult. Tong *et al.* (2025) report positive but variable effects across stem cell sources. Lambadiari *et al.* (2024) and Montague *et al.* (2024) indicate that cord blood-derived soluble products have clinical relevance in

diabetic wounds. Teng *et al.* (2022), Yan *et al.* (2022), and Yang *et al.* (2024) explain why cell-free signals influence inflammation, angiogenesis, collagen deposition, and oxidative stress.

This comparison leads to a practical conclusion for cryopreserved cord blood preparations. Their strongest translational position lies between classic cell therapy and conventional wound pharmacology. Academic framing should describe them as biologically active adjuncts with immunoregulatory, trophic, and homeostatic potential. This wording avoids reduction of these preparations to ordinary dressings and avoids unsupported claims of definitive regenerative treatment for diabetic complications. The available evidence supports a middle position, where cord blood-derived

products influence the biological quality of the wound bed and adjacent tissues. The metabolic dimension deserves separate treatment. Clinicians often approach diabetic foot as a local surgical problem because necrosis, phlegmon, ulceration, and infection demand urgent local action. The wound still exists inside a systemic disorder. Earlier clinical publications linked Cryocord-C and cord blood-derived preparations with improvement of wound cleansing, regression of inflammatory manifestations, reparative activation, and correction of selected biochemical and immune indicators, including protein fractions, immunoglobulins, circulating immune complexes, and natural protection antibodies (Popovych, 2005a, 2005b, 2006, 2014a, 2014b, 2014c). Chaudhari *et al.* (2022) describe experimental and clinical evidence for cord blood-derived cells in diabetes mellitus, while recognizing inconsistent results in some type 1 diabetes settings. This contrast helps set the boundary. Cord blood-derived therapy should not be presented as universal metabolic correction. The more defensible claim concerns partial support of the metabolic-inflammatory terrain that impairs wound healing, especially when hyperglycemia, protein imbalance, oxidative stress, and immune dysfunction persist despite conventional care.

A second source comparison defines the therapeutic window with greater precision. Lambadiari *et al.* (2024) provide clinical support for local cord blood platelet lysate gel in diabetic foot ulcer healing. Montague *et al.* (2024) extend the local regenerative model through combined serum and membrane use, while wound-bed quality and infection control remain central to interpretation. Yang *et al.* (2024) give an immune-cell-derived exosome mechanism focused on monocytes and macrophage polarization. Yan *et al.* (2022) emphasize oxidative stress and angiogenesis. These sources converge around one implementation rule: cord blood-derived products have the strongest rationale after active control of necrosis and infection, with monitoring of inflammation, perfusion, exudate, granulation quality, and systemic metabolic status. The third objective concerns clinical implementation. The evidence does not justify routine use in all diabetes complications. It supports selective use where standard treatment has addressed mechanical and infectious

barriers but wound biology remains unfavorable. The target group is defined by more than ulcer size or diabetes duration. More useful criteria include delayed granulation, persistent low-grade inflammation after sanitation, microcirculatory insufficiency, recurrent exudation without uncontrolled infection, slow epithelial edge movement, and biochemical signs of weak reparative reserve. In such cases, cryopreserved cord blood preparations can serve as part of an adjunctive biological module.

The hypothesis receives qualified support. Cryopreserved cord blood preparations have a plausible place in combined treatment of diabetes complications because current evidence confirms the therapeutic relevance of immunomodulation, angiogenesis, fibroblast and endothelial activation, extracellular matrix regulation, oxidative stress reduction, and metabolic-inflammatory support. The qualification matters. The level of evidence differs across product types. Clinical evidence is stronger for some stem cell and platelet lysate interventions than for many specific cryopreserved preparations. Experimental exosome studies explain mechanisms, but they do not create direct equivalence between vesicles, cells, serum, and cryopreserved products. Earlier cryomedical clinical work gives continuity and practical orientation, while current implementation needs controlled documentation, clear inclusion criteria, and defined outcome metrics.

4. Discussion

Cryopreserved cord blood preparations require staged clinical reasoning in diabetic complication management. The starting point is the wound or complication type after conventional treatment has created a controllable field. In diabetic foot syndrome, clinicians first perform debridement, drainage when indicated, microbiological control, systemic antibiotic planning, vascular assessment, glycemic correction, offloading, and evaluation of neuropathic and ischemic factors. A preparation with immunomodulatory and reparative activity has limited value if necrotic tissue remains dominant or if uncontrolled infection continues to destroy the local matrix. Cord blood-derived preparations are best interpreted as regulators of the transition from inflammation to repair. In practical

terms, clinicians need to decide whether the wound has become biologically ready for a regenerative adjunct. Readiness cannot be reduced to a visually clean surface. It requires reduced purulent discharge, stable local temperature, controlled edema, viable granulation islands, absence of spreading cellulitis, acceptable perfusion, and a systemic metabolic condition that does not keep disrupting repair. After

these conditions appear, cryopreserved cord blood preparation enters the treatment plan with a clear target. **Table 1** compares therapeutic formats that often appear under the broad label of regenerative or cord blood-associated therapy. The comparison separates product logic, expected action, and implementation limits, since these formats should not be treated as interchangeable.

Table 1: Typology of cord blood-derived and related biological preparations for diabetic tissue complications (compiled by the author based on Popovych, 2014, Chaudhari *et al.*, 2022, Lambadiari *et al.*, 2024, Montague *et al.*, 2024, Teng *et al.*, 2022, Yan *et al.*, 2022, and Yang *et al.*, 2024).

Therapeutic format	Main biological content	Dominant therapeutic logic	Best clinical placement	Main limitation
Cryopreserved cord blood serum preparation	Soluble proteins, immunoregulatory factors, trophic mediators	Modulation of inflammation and support of reparative balance	Adjunct after sanitation of infected diabetic lesions	Requires precise indication and standardized administration
Cord blood platelet lysate gel	Platelet-derived growth factors and soluble regenerative mediators	Local stimulation of granulation and epithelial repair	Chronic diabetic ulcer with controlled infection	Product composition and preparation protocol influence effect
Cord blood or umbilical cord-derived cellular therapy	Living cells with paracrine and immunological activity	Broad regenerative and angiogenic support	Selected severe or refractory cases under regulated protocols	Viability, dosing, safety, and regulatory control are demanding
Extracellular vesicle-based product	Exosomes carrying proteins, lipids, and regulatory RNA	Cell-free delivery of paracrine signals	Future adjunctive model for inflammation and angiogenesis control	Translation to standardized clinical use remains incomplete
Combined serum or tissue-product approach	Soluble mediators plus scaffold-like support	Simultaneous wound-bed signaling and structural support	Prepared wound bed with poor granulation	Infection risk and wound-bed selection require strict control

The table separates related products that carry different clinical burdens. Cryopreserved cord blood serum, platelet lysate, living cells, exosomes, and combined tissue products differ in risk profile, mechanism, and clinical controllability. For a surgical article, the most defensible pathway places cryopreserved preparations inside a controlled wound-management sequence. This placement corresponds to the earlier clinical line in which Cryocord-C and cord blood preparations were used after surgical intervention, sanitation of purulent-necrotic lesions, and stabilization of the diabetic wound process, with attention to reparative dynamics rather than isolated

product administration (Popovych, 2005a, 2005b, 2006, 2014a, 2014b). This position protects the argument from exaggerated regenerative claims and keeps the product tied to the clinical problem: a diabetic wound often fails because infection, ischemia, inflammation, and metabolic disorder continue to interact after local tissue removal.

Implementation should follow a decision sequence. First, the clinician classifies the dominant barrier to healing. One patient presents with necrosis and infection. Another patient presents with ischemia. A third patient has wound inertia after adequate debride-

ment. Cryopreserved cord blood preparations fit the third situation most clearly, and they can enter the first two only after the urgent causes have been controlled. Second, the clinician defines the intended effect before administration. Edema reduction, immune recalibration, wound cleansing, granulation acceleration, and metabolic-homeostatic support require different monitoring signs. Third, the team embeds treatment into a recordable protocol. Dose, route, frequency, wound status, microbiology, perfusion indicators, local temperature, exudate quality, granulation pattern, epithelial edge movement, and adverse reactions need consistent documentation.

Metabolic support requires cautious wording. Cord blood preparations should not be described as systemic correction for diabetic complications. The more

accurate interpretation concerns improvement of the conditions in which repair occurs. Cord blood-derived mediators can influence inflammatory proteins, oxidative stress, immune complexes, macrophage behavior, endothelial activity, fibroblast migration, and matrix organization. These mechanisms matter because diabetic wound healing depends on several biological layers at once. Glycemic correction alone does not restore tissue competence, while local surgery alone cannot neutralize systemic metabolic injury. Combined treatment has to connect both levels. Table 2 proposes monitoring metrics for clinical use. The table serves analytical planning and does not claim validated thresholds. It connects the expected mechanism of cord blood-derived preparations with observable clinical and laboratory signals.

Table 2: Monitoring framework for adjunctive use of cryopreserved cord blood preparations in diabetic complications (compiled by the author based on Popovych, 2014; Sun *et al.*, 2022; Shi *et al.*, 2024; Tong *et al.*, 2025; Lambadiari *et al.*, 2024; Montague *et al.*, 2024).

Monitoring domain	What should be tracked	Reason for inclusion	Interpretation logic
Surgical wound status	Necrotic residues, exudate character, odor, wound-bed cleanliness	Biological therapy requires a prepared wound surface	Persistent necrosis argues for renewed sanitation before adjunctive therapy
Local inflammation	Edema, erythema, pain dynamics, local temperature	Immunomodulation should reduce destructive inflammation	Improvement supports continuation within combined treatment
Reparative activity	Granulation quality, epithelial edge movement, wound area trend	Cord blood-derived mediators are expected to support repair	Slow response suggests ischemia, infection, or metabolic instability
Perfusion and oxygenation	Peripheral pulses, vascular imaging data, transcutaneous oxygen when available	Regeneration depends on microcirculatory capacity	Poor perfusion limits expected benefit regardless of product activity
Infection control	Culture data when indicated, systemic signs, need for antimicrobial escalation	Biological products should not mask uncontrolled infection	Deterioration requires reassessment of antimicrobial and surgical strategy
Metabolic-homeostatic profile	Glycemic stability, protein status, inflammatory markers available in routine care	Diabetes-related biochemical instability weakens repair	Unstable values explain delayed local response
Safety	Fever, allergic signs, local worsening, unexpected exudation, tissue reaction	Adjunctive biological treatment requires active risk surveillance	Adverse signals require suspension and diagnostic review

The monitoring logic moves the discussion from product enthusiasm to clinical accountability. A cryopreserved cord blood preparation should change the wound trajectory or improve biological conditions that sustain repair. If no change appears, repeated administration should not become automatic. The team should return to the dominant barrier: residual infection, perfusion deficit, pressure overload, uncontrolled hyperglycemia, protein-energy deficiency, renal dysfunction, or inadequate offloading. A staged implementation model follows six clinical steps. The first step is diagnostic and surgical qualification. The clinician determines whether the diabetic complication is infected, ischemic, neuropathic, mixed, or complicated by deep purulent spread. The second step is standard stabilization through debridement, drainage, antimicrobial therapy, glycemic management, vascular consultation, and offloading. The third step is biological readiness assessment, where the clinician checks whether destructive inflammation has decreased and reparative potential has begun to emerge. The fourth step is adjunctive administration of the cryopreserved cord blood preparation according to protocol. The fifth step is response monitoring, with comparison between clinical signs, available laboratory markers, and the intended therapeutic target. The sixth step is adjustment. Continuation requires improved wound trajectory or a more favorable systemic condition for repair.

This model leaves room for the older patent logic related to cryopreserved cord blood preparations without turning the article into a patent summary. Patents in this field support the existence of a developed therapeutic concept, especially when they formalize combinations of surgical treatment, diabetic complication correction, and cryopreserved biological agents. In academic writing, they should remain supportive, while the clinical argument should rely on peer-reviewed publications that describe Cryocord-C, cord blood preparations, surgical sanitation, anesthesiological support, and postoperative wound repair in diabetic foot syndrome and purulent-necrotic diabetic lesions (Popovych, 2005a, 2005b, 2006, 2014a, 2014b, 2014c; Akter *et al.*, 2025). The patent line related to cryopreserve biological preparations strengthens the applied surgical orientation of this topic. Patent No.

7937 UA formalized a method for treating diabetes complicated by diabetic microangiopathy, while Patent No. 25268 UA addressed complex treatment of purulent-necrotic stages of diabetic foot syndrome (Popovych *et al.*, 2005; Popovych, 2007). In the present article, these patent materials should be treated as evidence of an established therapeutic trajectory, whereas the main argument should remain grounded in peer-reviewed clinical and experimental literature.

The main limitation of the proposed interpretation lies in product heterogeneity. Umbilical cord blood serum, platelet lysate, mononuclear cells, mesenchymal stem cell derivatives, and exosomes are biologically related but not identical. Evidence obtained for one format cannot be transferred mechanically to another. Cryopreservation adds another layer because freezing, storage, thawing, and preparation protocols influence biological activity. Outcome selection creates a second limitation. Wound area reduction is useful, yet it does not capture infection control, recurrence risk, limb preservation, function, pain, quality of life, and metabolic resilience. A mature clinical protocol should track several domains at once. Future academic work should build targeted indications rather than broad promotional claims. Studies need to define which diabetic complications are biologically suitable, which preparation format is used, what dose and route are selected, and which outcomes correspond to the expected mechanism. The strongest candidates are complex diabetic wounds after adequate sanitation, recurrent slow-healing ulcers with controlled infection, and post-debridement wound beds that show poor transition to granulation despite appropriate standard care.

5. Conclusion

Cryopreserved cord blood preparations have a rational place in combined treatment of diabetes mellitus complications when clinicians link their expected effects to immune balance, repair activation, and metabolic-homeostatic support. The reviewed evidence connects cord blood-derived and related regenerative products with inflammatory modulation, angiogenesis, fibroblast and endothelial activity, extracellular matrix organization, oxidative stress reduction, and support of the local repair environment.

Different biological formats require separate interpretation. Cryopreserved cord blood serum preparations, platelet lysate gels, living cellular products, and extracellular vesicle-based strategies share a cord blood or perinatal biological origin, yet they differ in composition, controllability, safety profile, and clinical maturity. The safest academic position places cryopreserved preparations between conventional wound pharmacology and high-complexity cell therapy. The hypothesis is supported with restrictions. Cryopreserved cord blood preparations are most justified as adjunctive regulators of the post-sanitation wound environment, not as independent curative agents for diabetic complications. Their use should follow surgical sanitation, infection control, vascular assessment, metabolic stabilization, and wound-bed readiness evaluation. The proposed implementation model links administration to measurable clinical targets and monitoring domains. This position preserves continuity with earlier cryomedical surgical work and aligns the article with contemporary regenerative medicine evidence.

6. Acknowledgment

The author has no acknowledgments to declare.

7. Conflicts of Interest

The author declares no conflicts of interest.

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