

Comparative analysis of dural substitute autologous vs. semisynthetic collagen-based dura graft

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Abstract. – OBJECTIVE: The aim of the present study is to evaluate the success rate and safety of both auto-grafts and collagen-based semi-synthetic grafts in patients with dura defects.

PATIENTS AND METHODS: A prospective comparative study was conducted at the neurosurgery departments of different hospitals in Peshawar and Faisalabad. Patients were divided into two groups: A (autologous graft) and B (semi-synthetic graft). Dura graft autologous was applied in one group of patients with supratentorial brain surgery. Fascia lata was used, harvested from the lateral thigh, 3 to 5 cm long incision at the junction of the upper and middle one-third of the upper leg. A bone flap was implanted in the subcutaneous region in the abdominal part. Perioperative antibiotics were given to all the patients, and surgical drains placed intraoperatively were removed after 24 hours of surgery. In the second group, semi-synthetic dura grafts of 2.5x2.5 cm and 5x5 cm 7.5x7.5 cm sizes were used. Statistical analysis was performed using SPSS version v.20. Student's t-test was performed for the two groups to compare categorical variables, and the data were considered statistically significant at $p > 0.05$.

RESULTS: In this study, 72 patients of both genders were recruited. We observed that the Semi-synthetic collagen matrix had less surgical time. The mean difference in surgical duration was observed as 40 minutes. However, both groups reported statistically significant differences in terms of surgical duration (< 0.001). No case of infection was reported in both groups. The overall mortality ratio was 12%. Two male deaths were recorded due to cardiovascular disorders, while one death of a 42-year male was also recorded.

CONCLUSIONS: Based on the above findings, it may be concluded that using a semi-synthetic collagen substitute for dura repair is a simple, safe, and effective alternative to the autologous graft for dura repair in dura defects.

Key Words:

Autologous graft, Semi-synthetic graft, Dura defects.

Introduction

Dura defect and the subsequent leakage of CSF is considered an adverse complication of the brain and spinal surgery¹. Approximately 30% of thoracic myelopathy patients develop dura defects and a reduction in CSF levels. Generally, 2% of endoscopic lumbar discectomy cases reported dura defects². However, incident rates increased in cervical ossification patients ranging from 5% to 30% worldwide³. These defects can cause CSF pseudocyst, headache, post-operative infections, adhesive arachnoiditis, and cerebrospinal meningitis³.

Consequently, various scholars⁴ suggested that efficient repair of dura defects can significantly reduce the chances of post-operative infection, arachnoiditis, and neural damage. Dura mater plays a vital role in protecting CNS, modulating neural progenitors, modulating the survival rate of radial glial, and modulating axon behavior at the CNS-PNS interface. It is also required to function the dura mater properly and to avoid or reduce cerebrospinal fluid (CSF) leakage^{1,2}. Therefore, it is necessary to treat these defects immediately after identification. Various surgical interventions repair the dura mater, including periosteum, muscular fascia, and dura mater substitutes⁵. In many cases surgical interventions are quite hard not due to coagulation because they narrow down the dura and cause excisions during surgical procedures. So, dura substitutes are widely used for treating these defects⁵. The National Medical Product Administration of Chi-

na (NMPA) provides guidelines for dura mater substitutes. These guidelines recommended that substitutes should be biocompatible without prompting an inflammatory or immune response, reducing the chance of infections and inhibiting leakage of CSF⁶. Various dural substitutes used over the years are fascia lata, including semi-synthetic collagen-based dura grafts having certain advantages and limitations. Studies reported that fascia lata could cause morbidity at the donation site and require a minor incision^{7,8}.

Semi-synthetic collagen-based dura graft has several advantages, comprising non-toxic, degradable biomaterial with antibacterial properties. At the same time, semi-synthetic dura substitutes have yet to be fully studied and developed in terms of quality and impermeability⁵. Recently a study conducted by Xu et al⁹ investigated the efficacy of semi-synthetic collagen-based dura substitutes in animal models. Various approaches were used to perform a comprehensive analysis to identify dura mater substitutes in repairing dura mater defects. The results of the study showed no variation in body weight and temperature, and pyrogen reaction. Also, there was an insignificant variation in the leukocyte count. Similarly, Wang and Ao¹⁰ showed low chances of immunological responses and infection after using a semi-synthetic collagen matrix.

Autografts, for example, pericranium have obvious advantages; these are easy to use and economically favorable with suitable biological characteristics. However, patients with dura defects have damaged pericranium, which might not be sufficient for preparing the graft¹¹. Also, autologous fascia lata involves an additional incision during the surgery time and can be linked with complications. Many researchers advise using autologous substitutes; however, these days, neuroscientists do not favor using autologous substitutes as the process is time-consuming and requires the withdrawal of the galea-pericranium layer and then its subsequent use of sutures. Other than the autologous dura substitute, different xenografts have been identified, for instance, bovine pericardium and collagen matrix. However, xenograft use is linked with several side effects, including graft dissolution, body rejection, inflammatory responses, scarring, and adhesion formation^{12,13}.

Autologous dura substitutes and collagen-based grafts are currently considered suitable approaches for repairing dura defects, but no satisfactory clinical and functional outcomes have been ob-

tained yet. Still, there is a need to identify better surgical interventions regarding clinical and functional outcomes. The current study aimed to compare autologous dura substitute and collagen-based graft outcomes in patients with dura defects.

Patients and Methods

This prospective comparative study was conducted at the neurosurgery departments of different hospitals in Peshawar and Faisalabad to determine the appropriate treatment intervention for dura mater defect. Seventy-two patients of both genders were chosen using non-probability random sampling. Patients of supratentorial brain surgery requiring dura substitute aged above 20 years were included. All the cases of spine injury, infected wounds, pregnant women, and immunocompromised patients were excluded. The study was conducted after the approval of the Institutional Ethical Committee. Written informed consent was also taken from the patients' attendants. A pre-designed questionnaire recorded all the patients' information, including sociodemographic data, clinical data, and medical history.

Patients were randomly allocated into two groups. Group A undergoes dura repair with an autologous graft, while Group B undergoes dura repair with a semi-synthetic dura substitute. A single surgical team performed the whole procedure, and an experienced surgeon performed the procedure. CSF leakage and infection were noted after surgery and dural substitute either with autograft or semi-synthetic grafts. Then the patients were regularly followed up and examined for three months at the two-week interval. Computed tomography was performed to check the brain functioning and rule out complications, CSF leakage, and postoperative hemorrhage infection.

Dura graft autologous was applied in one group of patients with supratentorial brain surgery. Fascia lata was used, harvested from the lateral thigh, 3 to 5 cm long incision at the junction of the upper and middle one-third of the upper leg. A bone flap was implanted in the subcutaneous region in the abdominal part. Perioperative antibiotics were given to all the patients, and surgical drains placed intraoperatively were removed after 24 hours of surgery. In the second group, semi-synthetic dura grafts of 2.5x2.5 cm and 5x5 cm 7.5x7.5 cm sizes were used. The graft

Table I. Socio-demographic characteristics of participants.

	Group: A	Group: B
Mean age	40 years	36 years
Male	33 (91%)	30 (83%)
Females	3 (8%)	6 (16%)

was used according to the dura defect preoperatively. The technique was applied after rinsing the dura graft with normal saline.

Statistical Analysis

Statistical analysis was performed using SPSS version v.20 (IBM Corp., Armonk, NY, USA). Student's *t*-test (*t*-test) was performed for the two groups to compare categorical variables, and the data were considered statistically significant at *p*-value > 0.05. Descriptive and analytical statistics were presented in mean, average, and frequency. Pearson Chi-square was used for the comparison of proportions between the groups. All results were presented as tables and graphs.

Results

In this prospective comparative study, 72 patients with a mean age of 40.36 ± 5.5 years were included. Patients were randomly divided into two groups: A (autologous draft) and B (semi-synthetic collagen). A mean age of 40 years was observed in group A while group B consisted of patients with an average age of 36. The ratio of male participants was more than females in both groups. Group A had three females (8%) and 33 males (91%) participants, while group B contained six females (16%) and 30 males (83%). Detailed characteristics of patients are mentioned in Table I.

In group A, the mean surgical duration was comparatively higher than the Group B (180.143 ± 3.5 minutes vs. 130.143 ± 3.5 minutes), with a mean difference of 40 minutes. This time

difference indicated that a significant amount of time could be saved using a semi-synthetic collagen draft vs. an autologous graft. However, both groups reported statistically significant differences in terms of surgical duration (*p*-value < 0.001) (Table II). Autologous surgery required 16% more time for completion when compared with semi-synthetic collagen (3%). No case of infection was reported in both groups. After the surgery, all the patients were monitored in the intensive care unit and received antiepileptics and antiedema treatments. Physiotherapy was also done on all the patients. The overall mortality ratio was 12%. Two male deaths were recorded due to cardiovascular disorders, and one death of a 42-year male was also recorded. In group A, postoperative subcutaneous CSF collection was observed in 15% of cases resolved after one month of surgery. Both the substitutes showed similar results for dura adhesion; leakage of CSF was prevented. However, autologous grafts showed higher tightness than semi-synthetic collagen (Table III). Postoperative hospital stay was observed as 28 ± 1.5 hours, while Group: B was 25 ± 1.5 hours. No significant difference was recorded regarding the number of days the patient stays at the hospital (Figure 1).

This research was conducted to compare the outcomes of autologous vs. semisynthetic collagen-based graft in patients with dura mater defect. The present study revealed a significant reduction in the surgery time of semi-synthetic collagen. An overall time difference of 40 minutes was observed between both groups. These results are parallel to the previous study of Waheed et al¹³. In our autologous study group reported CSF leakage due to the employment of surgical dissection, which prolonged the hospital stay. Similar results were also reported by Li et al¹⁴.

Reconstruction of dura mater during spinal surgery should be done by using sutures to reduce the chances of CSF leakage because increased hydrostatic pressure is observed in the spine and lumbar region¹⁰. In the present study, reconstruc-

Table II. Statistical analysis of dura repair.

	Materials	Mean	Standard deviation	Standard error of mean
Surgery time in minutes	Autologous graft	180.03	3.64	0.87
	Semi-synthetic collagen	130.13	4.64	1.07
Dural separation time	Autologous graft	48.10	2.29	0.68
	Semi-synthetic collagen	26.17	2.21	0.66

Table III. Parameter evaluated post operatively.

	Autologous graft (N = 36) Mean score	Semi-synthetic collagen graft (N = 36) Mean score
Workability	3.0	2.2
Flexibility	2.0	2.1
Tightness	1.2	2.3
Overall evaluation	3.1	2.6

Following scores were given to patients immediately after the surgery, 1 = very good, 2 = good, 3 = acceptable, 4 = poor, 5 = not acceptable.

tions were performed without the use of sutures, and during the follow-up time, no CSF leakage was observed. Literature suggests that using autologous grafts was considered an effective and rapid technique for repairing dura defects unsuitable for typical suturing procedures. This technique can also be used for the reinforcement of suboccipital suture lines^{15,16}.

A study by Hida et al¹⁵ used bioabsorbable dural substitutes in 150 patients with dura defects who underwent the repair procedure. CSF leakage was observed in 7% of patients, and the authors identify this approach as an effective replacement for artificial dura substitutes.

A study by Narotam et al¹⁶ identified collagen matrix as a suitable approach for posterior fossa in which it was applied as a graft, without using sutures. The collagen matrix serves as a chemical stimulus for fibroblast infiltration, which begins on the 4th day and is established until the 14th day. The fibroblast serves as a scaffold for new collagen by adhering to the pores present in the matrix of collagen. At the end of 6 weeks

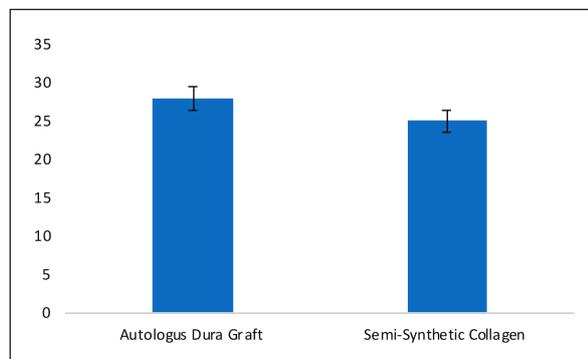


Figure 1. Hospital Stay of autologous dura graft and semi-synthetic collagen draft repair for dura defect.

matrix of collagen is completely absorbed and replaced by a new dura mater. Therefore, this approach has an efficient safety profile and is easy to use¹⁵.

Limitations

The current study has a few significant limitations as the small number of samples is also a significant concern that may raise the risk of type-2 error. The non-random, heterogeneous grouping and small sample size limit the analysis of both types of interventions that authenticates the current results. The major limitation of the current study is the small sample size with a short follow-up time. Larger sample size and more extended follow-up period are recommended to make more accurate results.

Conclusions

Based on the above findings, our study concluded that using a semi-synthetic collagen substitute for dura repair is a simple, safe, and effective alternative to the autologous graft for dura repair in dura defects. There is a significant reduction in surgery time, surgical trauma, and the number of days patients stay at the hospital using semi-synthetic collagen graft compared with autologous graft for dura repair.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Ethics Approval

Ethical approval was obtained from ethical committee of Lady Reading Hospital, Peshawar, Pakistan (Ethical approval No. 1424-B).

Informed Consent

Prior to study, informed consent was obtained from the patients after explaining them in their local language.

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Authors' Contribution

Conceptualization: Zahid Khan; Data curation: Zahid Khan, Sara Pervez, Seema Sharafat; Formal analysis: Sara Pervez; Investigation: Zahid Khan, Sara Pervez, Seema Sharafat; Project administration: Zahid Khan, Sara Pervez; Resource: Sara Pervez, Zahid Khan; Software: Seema Sharafat; Supervision: Zahid Khan; Validation: Seema Sharafat; Visualization: Sara Pervez; Writing – original draft: Sara Pervez, Zahid Khan; Writing – review & editing: Zahid Khan, Sara Pervez, Seema Sharafat.

Data Availability

The data will be available with corresponding author and can be obtained when necessary upon reasonable request.

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