

The Use of a Biodegradable Collagen/Vicryl Composite Membrane to Repair Partial Nephrectomy in Rabbits

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Summary. A composite membrane produced from collagen and vicryl mesh has been used to cover the kidney surface following partial nephrectomy in rabbits. The membrane readily held sutures, gave satisfactory haemostasis, and prevented leakage of urine. The experiments showed that the prosthesis biodegraded in less than twenty weeks. The only observed long-term effect of the material was thickening of the renal capsule. The results indicate that this membrane may be a suitable reparative material for use in traumatised kidneys in humans.

Key words: Collagen vicryl composite, Partial nephrectomy, Urinary tract repair, Rabbit.

Introduction

Collagen, due to its high tensile strength, biodegradability, low antigenicity, and other characteristics has found many applications in the biomedical field [3–5, 9–11, 17, 20]. Included in these properties is the ability to produce haemostasis and, because of this, collagen based haemostatic agents in the form of a sponge, powder or a fleece have proved useful when dealing with severe injury to soft organs such as liver [5, 18] and spleen [5, 14, 18].

We have successfully used a collagen membrane to seal experimental ureterotomies [16]. The material proved to be soft and tended to tear easily when wet, making suturing difficult. This surgical problem was subsequently overcome by reinforcing the collagen with Vicryl mesh to form a much stronger material. Vicryl mesh alone has shown promising results in other areas of operative surgery [1, 2, 12, 13] and it has been proposed from in-vitro experimentation that a combination of Vicryl mesh and collagen may well serve as a useful prosthetic material in the urinary tract [8].

The present study reports the use of this composite material to cover the operation site following partial nephrectomy in experimental animals.

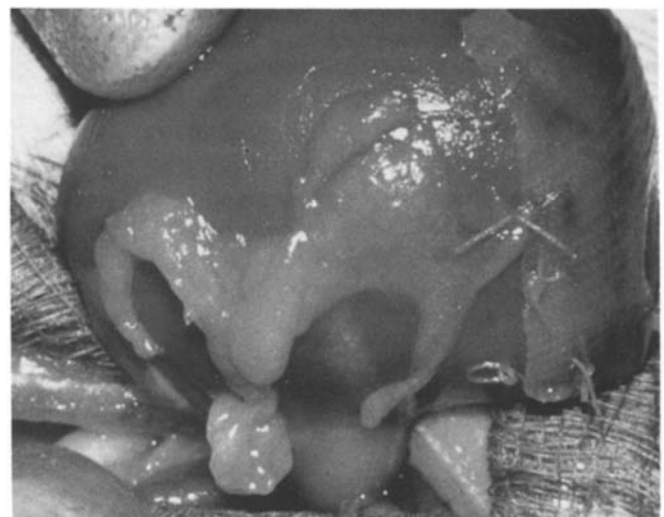


Fig. 1. Membrane sutured to partial nephrectomy site (x5)

Materials and Methods

Collagen coated Vicryl (polyglactin) Mesh was prepared as described in an earlier report [8] and the material was sterilised by immersion in 70% ethanol before use.

Adult male New Zealand White rabbits weighing 2.8–3.2 kg were used for the experiment. Each rabbit was given a 1 week course of Aureomycin followed by at least one week free of antibiotics before being submitted to operation. No peri or post-operative antibiotics were administered.

Anaesthesia was induced with 0.9 ml “Hypnorm” (Janssen Pharmaceuticals) administered by intramuscular injection into the rear hind leg, and immediately before operation the rabbits were shaved over the operation site. During the operation, anaesthesia was maintained using a mixture of nitrous oxide (60%), oxygen (40%), and halothane (1–2%) with the animal breathing spontaneously. Body temperature was maintained using a C. F. Palmer Haemothermic Blanket, and monitored using a rectal probe.

The left kidney was approached via a loin incision, and delivered into the wound; the vascular pedicle and ureter were identified and a portion of the lower pole of the kidney was amputated. Haemostasis was achieved using “finger-thumb” compression of the kidney

Table 1. Duration of experiments

Animal number	Sacrifice times (weeks)
1, 2	4 ¹ / ₂
3	6
4	8
5	10
6, 7, 8	12
9, 10	17
11, 12	20

Control experiments (suturing of material without nephrectomy to intact right kidney) were performed on animals 8–12 inclusive

while a 1.5 × 1.5 cm patch of collagen/vicryl composite was sutured to the existing capsule using 4/0 or 3/0 vicryl or dextron sutures (Fig. 1). The wound was then closed using vicryl or chromic catgut for the muscle layers and silk for the skin. Immediately following the operation, the rabbits were placed in a specially heated cage to recover from the anaesthetic.

In five animals, control experiments were carried out simultaneously when the right kidney was delivered, and a piece of collagen/vicryl composite (1.5 × 1.5 cm) sutured directly onto the lower pole without performing a partial nephrectomy.

A total of thirteen animals were used, one of which died a few hours after the operation from unrelated causes and is not included in the study.

The animals were sacrificed over a twenty week period as shown in Table 1, using an intravenous injection of sodium pentobarbitone (5 ml of a 200 mg/ml solution).

Following post-mortem examination, the kidneys were removed and fixed in neutral buffered formalin for routine histology. Sections for histology were processed using haematoxylin, phloxine, and saffron (HPS trichrome) staining.

Results

The general appearance and overall health of all the animals remained satisfactory over the duration of the experiments. There was no evidence to suggest bleeding or leakage of urine from the operation site in any animal.

Macroscopic (Post-mortem) Findings

There appeared to be little obvious macroscopic difference between the animals, despite differing intervals prior to sacrifice. In each case, the operative site could readily be identified on the left kidney as a flattened area overlayed with whitish scar tissue at the site of removal of the lower pole. The kidneys tended to be buried deeply in perinephric fat and adhesions to bowel and abdominal wall were common features; in one case at 4¹/₂ weeks, adhesions to the liver were observed.

The collagen vicryl composite could not be detected macroscopically in any of the animals, and a satisfactory repair of the nephrectomy site was observed in each case. No urinomas were found.

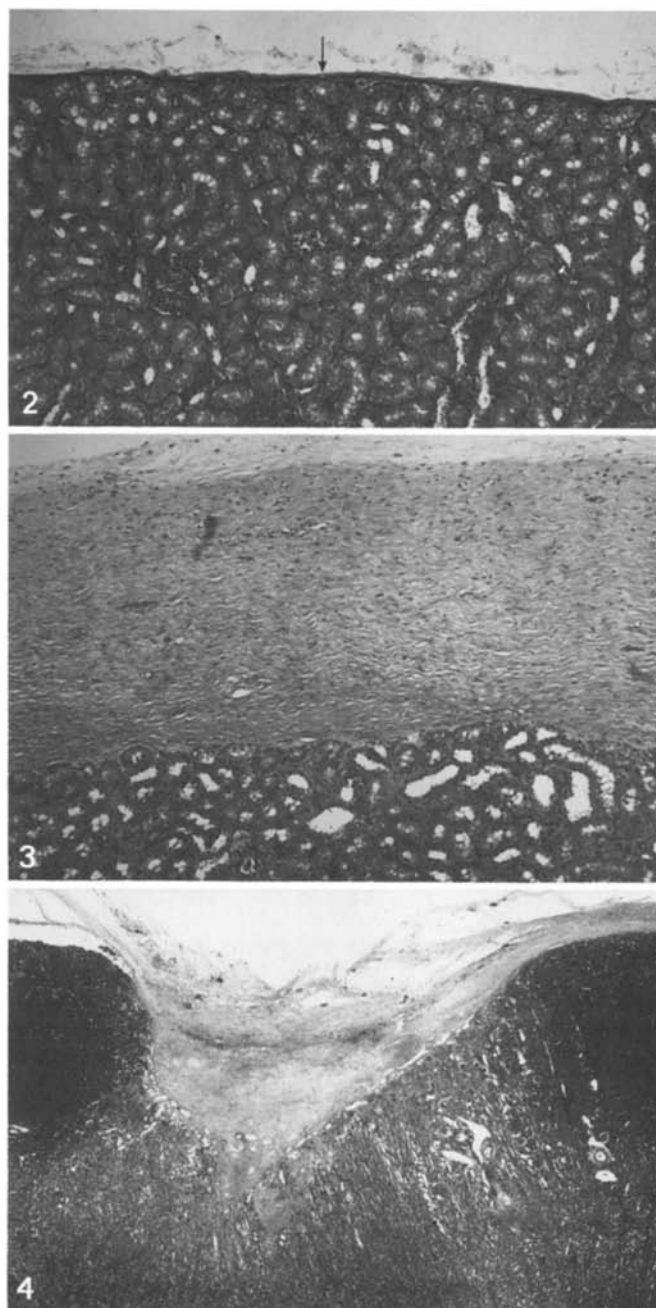


Fig. 2. Normal rabbit kidney showing renal capsule (indicated by arrow) (×150)

Fig. 3. Animal at twelve weeks showing thickening of the renal capsule. The membrane has completely disappeared (×150)

Fig. 4. Animal at eight weeks showing area of ischaemic fibrosis with tubular atrophy (×20)

Four animals showed signs of infection at post-mortem. In two partially nephrectomised rabbits, a large perinephric abscess was found in one animal at 4¹/₂ weeks and a small perinephric abscess at 20 weeks. In two control operations, one animal had a large perinephric abscess at 17 weeks, and another rabbit (also at 17 weeks) had a very small abscess.

Microscopic (Histological) Findings

Fig. 2 shows a normal rabbit kidney.

In all operated cases, the repair showed itself as a reconstituted capsule, which was much thicker than the original (Fig. 3).

The membrane biodegraded rapidly. In one animal sacrificed at 4½ weeks, distinct residues of the membrane were still visible but may have become detached from the operation site due to infection whereas in the other rabbit sacrificed at 4½ weeks, no sign of the membrane was present. In the partially nephrectomised kidneys only traces of collagen or vicryl were visible at 6, 8 and 12 weeks (in one animal only), but not at 17 and 20 weeks. In the control animals, minute traces of implant could be seen at 17 weeks but not at 12 or 20 weeks.

In all except one of the partially nephrectomised kidneys, (animal no. 10 at 17 weeks) areas of ischaemic fibrosis with tubular atrophy were observed, an example of which is shown in Fig. 4. In some animals this effect was more severe than others. Similar findings were also observed in two of the control kidneys (nos. 11 and 12 at 20 weeks) making it highly unlikely that the partial nephrectomy itself was the cause. It is thought that these areas represent classical wedge shaped regions of infarcted kidney substance which have arisen as a result of vascular occlusion. Signs of chronic inflammation were also detected in some of the kidneys.

Discussion

The collagen vicryl membrane proved to be easy to handle, strong enough to accept sutures, gave satisfactory haemostasis and prevented leakage of urine. The experiments have shown that the composite membrane will biodegrade without trace before 20 weeks (in many cases considerably earlier), with the only long-term pathological finding being a considerable thickening of the renal capsule.

The incidences of infection observed at post-mortem in two partially nephrectomised and two control kidneys may well be cause for some concern. However, it must be borne in mind that no post-operative antibiotic cover was administered to these animals, a situation which would be better controlled and assessed in human subjects.

Histologically, fibrotic tracts were found which were almost certainly caused by infarcts, the most probable cause of which was the "fingerthumb" method used to produce haemostasis which produced uneven areas of ischaemia. There was no evidence to suggest that such an effect was directly related to the presence of the membrane.

As early as 1968, Tanner et al. [19] had used a chemically cross-linked collagen film to cover the raw area of a heminephrectomy performed in the dog. After three weeks, the film became covered with a thin layer of connective tissue which became more dense after three months. After five months, the film had largely disappeared except in one

animal where traces of collagen could be demonstrated, and was replaced by a thick, but normal-appearing renal capsule. No collections of fluid or blood were found deep to the film, and very little renal atrophy adjacent to the film occurred. In a single human case of partial nephrectomy, the results were satisfactory using the tanned collagen film [19].

In the current study, we have used a non chemically cross-linked collagen which has been mechanically reinforced with a water soluble polyglactin mesh. This is stronger than a plain collagen film and will hold sutures without any difficulty. The absence of any chemical cross-linking means that the membrane will biodegrade faster than a tanned film and indeed our results show that at ten weeks the prosthesis had disappeared. In one of three animals at twelve weeks there were minute traces of the composite material, and tiny remnants in the control animals only at seventeen weeks. Even at four and six weeks, traces of implanted material were to be seen, and at twenty weeks, the membrane had disappeared completely. As in the earlier report [19] there was no collection under the membrane or any renal atrophy resulting from the composite material itself.

Conclusion

The collagen/Vicryl composite membrane is most effective as a substitute material which could, in the human situation, be applied to control haemorrhage and urinary leakage following partial nephrectomy. It could also prove to be a very useful material in the closure of nephrotomy incision following the removal of calculi from within the renal substance.

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