Heparin

Comparative effectiveness of fibrin sealants in cardiac surgery.

Authors: Arnold M.R., Ito D., Magee G., Xiong Y., Testa D., Rubinstein M., Tackett S.

Publication Date: 2015

Abstract:

Objectives: While effectiveness of fibrin sealants for controlling bleeding in cardiac surgery has been demonstrated, there is a paucity of research on other clinical outcomes of fibrin sealants. In this retrospective observational study we analyzed the clinical outcomes of two different fibrin sealants in a population of patients undergoing cardiac surgical procedures. Methods: Data from patients undergoing coronary artery bypass grafting (CABG), valve and valvular procedures with CABG during the years 2008 - 2012 were extracted from Premier's Hospital Database. The Premier Hospital Database is a comprehensive database containing data from over 6 million US hospital discharges annually. Only surgeries in which a fibrin sealant was utilized were included; all other hemostatic agents were excluded from the study. The following clinical outcomes were assessed: major and minor complications, transfusions, surgical revisions for bleeding, operative mortality (hospitalization), OR time and hospital and ICU length of stay (LOS). Logistic regression analyses were performed on categorical outcome variables and GLM regression analyses were performed on continuous outcome variables. Study covariates included: age, primary procedure, Charlson Co-morbidity Index (CCI) score, heparin use, protamine use, admission type, gender, race, teaching hospital, bed size and region. Results: A total of 2,560 inpatient cardiac procedures using fibrin sealant with synthetic aprotinin (FS-apr) were compared to 1,019 procedures using fibrin sealant without aprotinin (FS). Results suggested that FS-apr was associated with significantly lower rates of minor complications (21.1% vs. 27.1%, $p = 0.002$), Day 1 Transfusions (28.6% vs. 36.8%, $p = 0.015$) and ICU LOS (4.7 days vs 7.1 days, $p < 0.0001$) as compared to FS. No significant differences were found between FS-apr and FS on the other clinical outcomes. Conclusions: FS-apr

was associated with signficantly lower rates of Day 1 Transfusions, avoidable minor complications and lower average ICU LOS as compared to FS.

Closure of guide wire-induced coronary artery perforation with a two-component fibrin glue.

Authors: Storger H., Ruef J.

Publication Date: 2007

Abstract:

Perforation or rupture of a coronary artery with subsequent pericardial effusion and cardiac tamponade is a potentially life-threatening complication of percutaneous coronary intervention (PCI). Several emergency treatment strategies exist to close the perforation including reversal of anticoagulation, prolonged balloon inflation, implantation of stent grafts, local injection of thrombogenic molecules, placement of microcoils, or open heart surgery. Here we report on a 66-year-old patient who underwent urgent PCI for acute stent thrombosis in the proximal LAD. The artery was reopened, a new stent implanted successfully, and a GPIIb/IIIa-antagonist was given. Shortly thereafter the patient suffered from cardiac tamponade requiring pericardiocentesis and pericardial drainage. The coronary angiogram indicated a severe guide wire-induced perforation and pericardial effusion originating from a distal diagonal branch segment. Prolonged balloon inflation did not stop the leakage. Therefore the monorail balloon was exchanged for an over-the-wire balloon. A two-component commercial fibrin glue consisting of fibrinogen and thrombin was rapidly but separately injected through the wire channel of the balloon into the distal segment of the diagonal branch. The coronary leak was successfully closed and the patient recovered quickly. In comparison with the previously reported cases of thrombin injection important differences should be noticed: (1) a two-component hemostatic seal was used without reversal of anticoagulation, (2) rapid injection instead of prolonged infusion of the hemostatic drugs was performed, and (3) the rescue technique was applied in a cath lab that routinely uses monorail catheter systems. Therefore we consider this a novel and effective approach for closure of coronary ruptures.

Inc.

Preparation of autologous fibrin glue from pericardial blood.

Authors: Kjaergard H.K., Weis-Fogh U.S., Thiis J.J.

Publication Date: 1993

Abstract:

To salvage patients' blood and improve hemostasis in cardiac operations, autologous fibrin glue was prepared in a new way by means of ethanol from pericardial blood. The yield from 44 mL of blood was 2.1 +/- 0.7 mL (mean +/- standard deviation) of fibrinogen concentrate with a concentration of 25.1 +/- 7.5 mg/mL; 2.7 mL of two-component glue was obtained after the addition of thrombin solution. The glue has the advantages of safety from transmission of viral diseases and from immunologic reactions.

Tissue glue for sealing plastic valves and bioprosthesis in the canine aorta.

Authors: Saggau W., Hatipoglu O., Mittman U., Spath J., Storch H.H., Schmitz W., Wurster K.

Publication Date: 1982

Abstract:

In experiments on seven dogs, a fibrin glue was used to seal plastic valves and bioprosthesis in the thoracic aorta. Each valve was fixed in place with only four single sutures. Intraoperative and postoperative angiographic checks, with countercurrent aorta filling, gave no indication of perivalvular leak, even after eight weeks. Histologic studies confirmed the angiographic findings and showed only slight changes in the aortic wall. The results indicate that application of fibrin glue, supplementary to conventional suture procedure, may be useful when satisfactory fixation of aortic valves is hampered by pathologic circumstances.

Vascular endothelial growth factor delivered by fibrin glue accelerating arterial endothelialization.

Authors: Bian J.-F., Wang X.-L., Ma Z., Yao Q., Zhang J.-L., Wang T.

Publication Date: 2005

Abstract:

Background: Clinical efficacy of vascular therapeutic intervention is limited by the resultant de-endothelialization, thrombogenecity and intimal hyperplasia. Objective: To evaluate the effect of fibrin glue (FG) containing vascular endothelial cell growth factor (VEGF) on re-endothelialization, cellular proliferation and intimal hyperplasia by using canine model of balloon angioplasty. Design: A randomized controlled repeated measurement design. Setting: Department of Vascular Surgery; Institute of Neurosurgery, Xijing Hospital, Fourth Military Medical University of Chinese PLA. Materials: The study was carried out in the Institute of Neurosurgery, Xijing Hospital Affiliated to Fourth Military Medical University of the Chinese PLA, between October 2002 and June 2004. Fifteen healthy adult mongrel dogs of either gender, with body mass of 12.5 to 18.9 kg, were provided by the Surgery Laboratory for Experimental Animals, Xijing Hospital. Methods: In the bilateral carotid artery, FG/VEGF/heparin of one side was set as treatment group and the other side was set as control group. The intimal injury and the treatment results were observed at three time points 10, 30 and 90 days after injury. Thickness of vascular intima and medial layer was measured with Bioquant BQ OS/2 computer morphology measuring instrument. Cell proliferation rate was quantitated by 5-bromodeoxyuridine (BrdU) incorporation by immunohistochemistry. BrdU positive cells were counted using 40 x magnification. Scanning electron microscopy (SEM) was used to evaluate the percentage of endothelial cell coverage on the luminal surface. Main outcome measures: Coverage of endothelial cells, neointimal and medial thickness, and cellular proliferation. Results: All the dogs survived till the collection of samples with no loss in the midway. 1 Coverage

rate of endothelial cells: The arterial coverage rate at the treated side at days 10 and 30 was significantly higher than that at the control side [(66.73+/-30.78)%, (40.8+/-27.74)%, P=0.04; (96.67+/-10.29)%, (82.07+/-22.82)%, P=0.048]. 2 Proliferation of each vascular layer. It reached the peak at day 10 and recovered to normal at day 90. Compared with that of control group, cellular proliferation rate of neointima and the 1/2 of inside of media as well as media was significantly increased [(7.41+/-6.75)%, (3.56+/-2.72)%; (2.81+/-2.65)%, (0.83+/-0.59)%; (2.06+/-1.81)%, (0.62+/-0.31)%, $P < 0.05$]. 3 Thickness of neointima; Compared with that of control group, the thickness of intima/thickness of medial layer in both the proximal and the middle segments was significantly increased (0.18+/-0.22, 0.10+/-0.06; 0.21+/-0.23, 0.14+/-0.14; 0.12+/-0.08, 0.09+/-0.08; 0.29+/-0.40, 0.12+/-0.12, $P < 0.05$, $P < 0.01$), but there was no change in the distal segments. Conclusion: FG can distribute cytokines into the wall of injured arteries and retain the biological function of cytokines. VEGF plus heparin delivered by FG accelerates re-endothelialization concomitant with the proliferation of smooth muscle cell and intimal hyperplasia.

Polyglycolic acid felt sealing method for prevention of bleeding related to endoscopic submucosal dissection in patients taking antithrombotic agents.

Authors: Fukuda H., Yamaguchi N., Isomoto H., Matsushima K., Minami H., Akazawa Y., Ohnita K., Takeshima F., Shikuwa S., Nakao K.

Publication Date: 2016

Abstract:

Background and Study Aims. When performing endoscopic submucosal dissection (ESD) for patients on antithrombotic agents, the frequency of delayed bleeding is expected to increase. The endoscopic polyglycolic acid (PGA) felt and fibrin glue sealing method could be a new method for prevention of delayed bleeding. Patients and Methods. The safety and efficacy of the endoscopic tissue sealing method with PGA sheets and fibrin glue for the prevention of post-ESD bleeding were examined in 104 patients taking antithrombotic agents. During the study period, 70 patients taking antithrombotic agents did not undergo the sealing method, 36 patients discontinued antithrombotic agents, and 724 patients had not received antithrombotic therapy. Results. Delayed bleeding rates were 3.8% (4/104) in the sealing group, 12.9% (9/70) in the nonsealing group, 8.3% (3/36) in the discontinuation group, and 4.6% (33/724) in the nonantithrombotic therapy group. Thus, the delayed bleeding rate was significantly lower in the sealing group than in the nonsealing group and comparable to that in the nonantithrombotic therapy group. Conclusions. This PGA felt and fibrin glue sealing method might become a promising post-ESD bleeding prevention method in patients taking antithrombotic agents (UMIN000013990, UMIN000013993).

Hemostatic efficacy of EVARRESTTM, fibrin sealant patch vs. TachoSil in a heparinized swine spleen incision model.

Authors: Matonick J.P., Hammond J.

Publication Date: 2014

Abstract:

Background: First-generation single-component hemostats such as oxidized regenerated cellulose (ORC), fibrin, collagen, and gelatin have evolved into second and third generations of combination hemostats. Objective: This study compares two FDA approved products, EVARRESTTM, Fibrin Sealant Patch, a hemostat comprised of a matrix of nonwoven polyglactin 910 embedded in ORC coated with human fibrinogen and thrombin to TachoSil medicated sponge, an equine collagen pad coated with human fibrinogen and thrombin.

Materials and Methods: Swine were anticoagulated with heparin to 3X their baseline activated clotting time and a 15 mm long x 3 mm deep incision was made to create a consistent moderate bleeding pattern. Test material was then applied to the wound site and compressed manually for 3 min with just enough pressure to prevent continued bleeding. Hemostatic effectiveness was evaluated at 3 min and 10 min.

Results: At 3 min, the hemostasis success rate was 86% in the EVARRESTTM group and 0% in the TachoSil group, $p < .0001$. The overall success rate at 10 min was 100% with EVARRESTTM and 4% with TachoSil, $p < .0001$. Adhesive failure, in which the test material did not stick to the tissue, occurred in 96% of TachoSil sites. In contrast, 100% of the EVARRESTTM applications adhered to the test site.

Conclusions: EVARRESTTM, Fibrin Sealant Patch demonstrated greater wound adhesion and more effective hemostasis than TachoSil. Adhesive failure was the primary failure mode for TachoSil in this model.

The laparoscopy splenic injury repair. The use of fibrin glue in a heparinized porcine model. [Portuguese]

Authors: Freire D.F., Taha M.O., Soares J.H., Simoes M.J., Fagundes A.L.N., Fagundes D.J.

Publication Date: 2011

Abstract:

Purpose: To investigate the effectiveness of fibrin glue (laparoscopic via) into promote the hemostasis of a spleen injury on a heparinized porcine model. Methods: Eighteen Landrace porcine were submitted to laparoscopic spleen injury and randomly distributed: GHA (heparin plus adhesive), GH (heparin without adhesive) and GS (Sham - without heparin or adhesive). Ten minutes before the surgical procedures a single IV dose (200UI/kg) of heparin sodium was administrated only to groups GHA and GH. In the GHA, adhesive was applied after the mechanical injury and recorded the time until the polymerization and clot formation. Results: No significant differences occurred among the groups (Fisher test) considering the weight and surgery time. The blood amount in the abdominal cavity on GH was significantly higher in comparison to the sham group and especially with the GHA ($p<0.004$). No significant differences were observed in the body temperature, heart rate, cardiac output, means arterial pressure, pulmonary artery pressure during the experiment. The activated partial thromboplastin time (APTT) was lower in the GHA in comparison to GH ($p<0.003$). Conclusion: The fibrin biological adhesive applied by laparoscopy is effective for hemostasis of minor spleen injury in a porcine model under the effect of anticoagulant drug.

Randomized clinical trial of tranexamic acid-free fibrin sealant during vascular surgical procedures (Br J Surg 2010; 97: 1784-1789).

Authors: Hickey N.C.

Publication Date: 2010

Abstract:

Not Available

A modified technique of renal artery anastomosis in rat kidney transplantation.

Authors: Zhang G., Zhao H., Sun Z.-Y.

Publication Date: 2010

Abstract:

Aims: To reduce warm ischemic time and avoid irreversible damage to the graft in rat kidney transplantation. Methods: After left nephrectomy, recipients were transplanted with syngeneic kidney grafts using microsurgical techniques. In control rats (n = 20), the renal artery anastomoses were performed with 8-9 interrupted sutures by the conventional technique. In experimental animals (n = 20), a modified anastomosis was performed using fewer (5-6) sutures and fibrin glue devoid of thrombin. Results: The number of sutures in the control group was 8.09 +/- 0.35 while that in the experimental group was 5.65 +/- 0.48 ($p < 0.01$). The warm ischemic time reduced from 29.7 +/- 1.1 min in the control group to 23.9 +/- 0.9 min in the experimental group ($p < 0.01$). These anastomoses maintained adequate patency rates and mechanical strength. Up to 21 days after operation, the graft survival rates in the experimental and control groups were 90 and 85%, respectively. Conclusions: Our modified technique for renal artery anastomosis significantly reduced the warm ischemic time in rat kidney transplantation. This technique would be a safe and reliable method for rat renal artery anastomosis as well as for other microarterial anastomoses, particularly for novice surgeons.

An alternative method of vein anastomosis with fibrin glue [1].

Authors: Uysal A.C., Uraloglu M., Orbay H., Ortak T., Sensoz O.

Publication Date: 2005

Abstract:

Not Available

Prevention of bleeding after islet transplantation: Lessons learned from a multivariate analysis of 132 cases at a single institution.

Authors: Villiger P., Ryan E.A., Owen R., O'Kelly K., Oberholzer J., Saif F.A., Kin T., Wang H., Larsen I., Blitz S.L., Menon V., Senior P., Bigam D.L., Paty B., Kneteman N.M., Lakey J.R.T., Shapiro A.M.J.

Publication Date: 2005

Abstract:

Islet transplantation is being offered increasingly for selected patients with unstable type 1 diabetes. Percutaneous transhepatic portal access avoids a need for surgery, but is associated with potential risk of bleeding. Between 1999 and 2005, we performed 132 percutaneous transhepatic islet transplants in 67 patients. We encountered bleeding in 18/132 cases (13.6%). In univariate analysis, the risk of bleeding in the absence of effective track ablation was associated with an increasing number of procedures (2nd and 3rd procedures with an odds ratio (OR) of 9.5 and 20.9, respectively), platelets count <150 000 (OR 4.4), elevated portal pressure (OR 1.1 per mm Hg rise), heparin dose >=45 U/kg (OR 9.8) and pre-transplant aspirin (81 mg per day) (OR 2.6, p = 0.05). A multivariate analysis further confirmed the cumulative transplant procedure number (p < 0.001) and heparin dose >=45 U/kg (p = 0.02) as independent risk factors for bleeding. Effective mechanical sealing of the intrahepatic portal catheter tract with thrombostatic coils and tissue fibrin glue completely prevented bleeding in all subsequent procedures (n = 26, p = 0.02). We conclude that bleeding after percutaneous islet implantation is an avoidable complication provided the intraparenchymal liver tract is sealed effectively.

Fibrin Sealant Improves Hemostasis in Peripheral Vascular Surgery: A Randomized Prospective Trial.

Authors: Burks S.G., Gagne P.J., Kagan S.A., Lawson J.H., Spotnitz W.D., Aburahma A.F., Schenk III W.G.

Publication Date: 2003

Abstract:

Objective: To evaluate the efficacy and safety of an investigational fibrin sealant (FS) in a randomized prospective, partially blinded, controlled, multicenter trial. Summary Background Data: Upper extremity vascular access surgery using polytetrafluorethylene (PTFE) graft placement for dialysis was chosen as a reproducible, clinically relevant model for evaluating the usefulness of FS. The FS consisted of pooled human fibrinogen (60 mg/mL) and thrombin (500 NIH U/mL). Time to hemostasis was measured, and adverse events were monitored. Methods: Consenting adult patients (n = 48) undergoing placement of a standard PTFE graft were randomized in a 2:1:1 ratio to the treatment group using FS (ZLB Bioplasma AG, Bern, Switzerland), oxidized regenerated cellulose (Surgicel, Johnson & Johnson, New Brunswick, NJ), or pressure. Patients received heparin (3,000 IU IVP) before placement of vascular clamps. If the treatment was FS, clamps were left in place for 120 seconds after the application of study material to permit polymerization. If treatment was Surgicel, clamps were left in place until the agent had been applied according to manufacturer's instructions. If the treatment was pressure, clamps were released as soon as the investigator was ready to apply compression. Immediately after release of the last clamp, the arterial and venous suture lines were evaluated for bleeding. The time to hemostasis at both the venous and arterial sites was recorded. Results: Significant (P <= .005) reduction in time to hemostasis was achieved in the FS group. Thirteen (54.2%) patients randomized to FS experienced immediate hemostasis at both suture lines following clamp removal compared to no patients using Surgicel or pressure. Only

one patient (7.1%) in the Surgicel group and no patients in the pressure group experienced hemostasis at 120 seconds from clamp removal, compared to 13 (54.2%) patients for FS. Adverse events were comparable in all groups. There were no seroconversions. Conclusions: FS achieved more rapid hemostasis than traditional techniques in this peripheral vascular procedure. FS use appeared to be safe for this procedure.

Characterizing fibrin glue performance as modulated by heparin, aprotinin, and factor XIII.

Authors: Marx G., Mou X.

Publication Date: 2002

Abstract:

We describe the performance of fibrin glue (FG) as modulated by heparin, aprotinin, or factor XIII levels. In vitro tests and a rat kidney excision model demonstrated that the hemostatic efficacy of fibrin was not modulated by aprotinin. Overlapping rat skin sections demonstrated that adhesion strength (AS) was proportional to the area of overlap as well as to fibrinogen levels. AS was not modulated by exogenous heparin or aprotinin and was independent of the endogenous factor XIII in fibrinogen. SDS-PAGE developed by Coomassie or Western blots with anti-gamma chain antibody confirmed that normal skin sections contain adequate trans-glutaminase to maximally cross-link normal, as well as XIII-depleted, fibrin. Fibrin glue (FG) sprayed onto rat skin incision wounds with a dual channel spray applicator acted in 2 phases: initially (day 1), compared to wounds stapled without or treated with only thrombin, FG significantly increased breaking strength. In the second phase of wound healing (after day 3), all groups achieved increased but equivalent breaking strength. FG containing aprotinin (to 3000 U/m; Immuno, Behringwerke, Germany) exhibited initial tissue bonding strength equivalent to fibrin without aprotinin, but histological examination showed delayed fibrinolysis and a concomitant slower regeneration of granulation tissue. Thus, our data indicated that aprotinin was not particularly beneficial to wound healing and that the endogenous factor XIII level in the fibrinogen did not contribute significantly to skin bonding. Rather, the tissue supplied adequate trans-glutaminase activity required to crosslink fibrin to itself and to the tissue.

Reduction of hemorrhage after knee arthroplasty using cryo-based fibrin sealant.

Authors: Curtin W.A., Wang G.J., Goodman N.C., Abbott R.D., Spotnitz W.D.

Publication Date: 1999

Abstract:

The spray application of cryo-based fibrin sealant was evaluated for reducing hemorrhage in a complex, anticoagulated canine model of knee joint arthroplasty. Nine heparinized dogs underwent bilateral knee arthroplasty under tourniquet control with each animal having 3 mL of fibrin sealant sprayed onto one joint and the other joint serving as control. The fibrin sealant significantly reduced total and incremental bleeding as compared to the control side ($P < .05$). In addition, the hemostatic effectiveness of the fibrin sealant increased as bleeding propensity increased ($P < .05$). This study suggests that fibrin sealant may reduce bleeding from orthopedic joint replacement in human patients undergoing routine operations as well as those receiving forms of anticoagulation to reduce the incidence of deep venous thrombosis and pulmonary embolus.

Platelet deposition on ePTFE grafts coated with fibrin glue with or without FGF-1 and heparin.

Authors: Zarge J.I., Gosselin C., Huang P., Greisler H.P.

Publication Date: 1997

Abstract:

Introduction. The disappointing long-term patency of small-caliber prosthetic grafts may be due in part to early thromhogenicity of the prosthetic surface. We previously reported that the coating of expanded polytetrafluoroethylene (ePTFE) with fibrin glue (FG) containing fibroblast growth factor type 1 (FGF-1) and heparin accelerated spontaneous endothelial coverage of ePTFE grafts in an animal model; however, FG's effect on platelets remains unclear. This study was done to evaluate platelet deposition onto FG/FGF-1/heparin-coated vs FG-coated vs whole-blood- preclotted ePTFE surfaces. Methods. Twelve 5-cm ePTFE grafts were treated either with FG (thrombin, 0.32 U/ml, and fibrinogen, 32.1 mg/ml, n = 8) or with FG containing FGF-1 (11 ng/ml) plus heparin (250U/ml, n = 4). Twelve control ePTFE grafts were preclotted with canine (n = 8) or human (n = 4) whole blood. These treated grafts were placed onto a loop pulsatile perfusion system in pairs (preclotted with either FG or FG/FGF-1/heparin) and perfused with a M-199/10% FBS/¹¹¹indium-labeled platelet suspension. After 60 min the grafts were gamma counted and CPM/mm² were determined. Results. In both trials, the preclotted ePTFE grafts demonstrated similarly increased platelet deposition when compared to grafts treated with FG/FGF-1/heparin or FG alone ($P < 0.001$ for each). Conclusion. The decrease in platelet deposition on the FG/FGF-1/heparin-coated grafts vs preclotted grafts is not due to heparin and is not specific to canine or human platelets. FG-coated grafts may induce a decrease in early graft thrombogenicity when compared to whole blood preclotting.

Fibrin glue containing fibroblast growth factor type 1 and heparin decreases platelet deposition.

Authors: Zarge J.I., Husak V., Huang P., Greisler H.P.

Publication Date: 1997

Abstract:

BACKGROUND: The early success rates of endarterectomy and angioplasty are influenced by the thrombogenicity of the deendothelialized surface. We previously reported decreased platelet deposition after 30 and 120 minutes and after 28 days on expanded polytetrafluoroethylene (ePTFE) grafts coated with fibrin glue (FG) containing fibroblast growth factor type 1 (FGF-1) and heparin in canine aortoiliac bypass grafts when compared with control uncoated grafts. The FG/FGF-1/heparin coating has been shown to enhance spontaneous endothelialization at 28 days in canine ePTFE bypass grafts. The current study evaluates the thrombogenicity of this FG/FGF-1/heparin suspension applied to a balloon de-endothelialization model of endarterectomy in canine carotid arteries. METHODS: Nine dogs underwent bilateral, deendothelialization balloon injury to 6-cm segments of their carotid arteries. Fibrin glue (fibrinogen 32.1 mg/mL + thrombin 0.32 U/mL) containing FGF-1 (11 ng/mL) and heparin (250 U/mL) was applied to the luminal surface of one carotid artery in each dog. Both femoral arteries were circumferentially dissected but not balloon injured; one femoral artery was clamped for the same period as the carotid arteries. In the 6 acute dogs, 10 minutes prior to the restitution of flow in both carotid arteries and one femoral artery, 4 to 8 x 10⁹ ¹¹¹In-labelled autologous platelets were injected intravenously. Four-cm segments of both carotid and femoral arteries were excised after 15 or 120 minutes of circulation (n = 3/time/artery, 24 arteries). In the 3 chronic dogs, the radiolabelled platelets were injected 30 days after carotid injury. The carotid and femoral vessels were then excised after 120 minutes of perfusion. Radioactive platelet deposition was quantitated by gamma counting.

RESULTS: After 2 hours, the injured carotid arteries demonstrated significantly more platelet deposition than either uninjured femoral artery controls ($P < 0.001$). There was also a significant 45.2% decrease ($P = 0.008$) in platelet deposition on the balloon injured carotid arteries treated with FG/FGF-1/heparin when compared with balloon injured carotid arteries alone. At 30 days there was an insignificant trend toward decreased thrombogenicity in the FG/FGF-1/heparin treated injured carotids. CONCLUSION: Surface coating with FG/FGF-1/heparin significantly decreases platelet deposition on balloon injured canine carotid arteries after 2 hours of perfusion and may be clinically applicable in endarterectomy and angioplasty procedures. The long- term induction of reendothelialization of arterial surfaces by this technique is under investigation.

Restoring lens capsule integrity enhances lens regeneration in New Zealand albino rabbits and cats.

Authors: Gwon A., Gruber L.J., Mantras C.

Publication Date: 1993

Abstract:

In studies conducted by numerous investigators for 150 years, lenses regenerated following endocapsular lens extraction in New Zealand albino rabbits have been irregular in shape, appearing primarily doughnut-shaped as a result of lack of lens growth at the site of the anterior capsulotomy and its adhesion to the posterior capsule. In the present study, we restored the lens capsule integrity by inserting a collagen patch at the time of surgery to seal the anterior capsulotomy and to improve the shape and structure of the regenerated lenses. We then filled the capsule bag with air to prevent adhesions between the anterior and posterior capsule and maintain capsule tautness and shape. Lens regeneration was first noted as early as one to two weeks. Regenerated lens filled approximately 50% of the capsule bag at two weeks and 100% by five weeks. Subsequent growth was in the anterior-posterior direction and measured by A-scan biometry. Lens thickness increased by 0.3 mm per month. The regenerated lenses were spherical with normal cortical structure and a nuclear opacity. In conclusion, restoration of lens capsular integrity with a collagen patch following endocapsular lens extraction enhanced the shape, structure, and growth rate of the regenerated lenses. In addition, lens regeneration was shown to occur in two cats.

Graft hemostasis of fibrin glue from cryoprecipitate of autologous FFP. [Japanese]

Authors: Shimazu A., Odagiri S., Ishikura Y., Sakamoto H.

Publication Date: 1991

Abstract:

Not Available

Preparation of fibrin glue from single-donor fresh-frozen plasma.

Authors: Dresdale A., Rose E.A., Jeevanandam V.

Publication Date: 1985

Abstract:

Fibrin glue is used widely in Europe as a tissue sealant and hemostatic agent. The European glue is prepared commercially from pooled human blood. It is not available in this country because of the risk of transmission of hepatitis B, acquired immune deficiency syndrome, and other blood-transmitted diseases. We describe a cryoprecipitation technique for preparation of fibrin glue from single-donor fresh-frozen plasma. This technique enables the glue to be made in large quantities with no greater risk of disease transmission than with that from the transfusion of single-unit fresh-frozen plasma. We have found that the glue is a useful tool in surgery. By helping to control difficult bleeding, its use can decrease the need for blood transfusions and shorten operating room time. It also is effective as a means to pretreat highly porous vascular prostheses that currently are used infrequently because of bleeding. These porous grafts offer potential advantages in handling, suturing, and long-term patency. This new technique of fibrin glue preparation may make this useful surgical adjunct as readily available in this country as it is in Europe.

Use of fibrin sealant for reinforcing arterial anastomoses.

Authors: Jakob H., Campbell C.D., Qiu Z.-K.

Publication Date: 1984

Abstract:

Not Available

The effect of heparinized fibrin-glue in the vascular surgery with Dacron graft. [Japanese]

Authors: Matsuda M., Tabata R., Mori A., Okada Y.

Publication Date: 1984

Abstract:

Not Available

Use of Quixil human surgical sealant in achieving hemostasis on a skin graft recipient site of a fully heparinized patient.

Authors: Ali SN, Moiemen NS

Publication Date: 2006

Abstract:

Not Available

Commercial fibrin sealants are not equivalent in a rabbit liver-resection model which quantitatively evaluates hemostasis and formation of adhesions.

Authors: Nur I, Lyahovetsky Y, Bar L, Schon M

Publication Date: 2005

Abstract:

A rabbit partial liver resection model was used to determine the hemostatic effectiveness of a new fibrin sealant. Persistent bleeding, with a mean bleeding time of 372 s and blood loss of 18 ml, from a resected lobe of the liver was achieved after rabbits in the untreated control group had been infused continuously with unfractionated heparin over 20 min with 0.2 IU/ml at a rate of 1 ml/min. Spraying the resected surface with the new fibrin sealant, Quixil, reduced bleeding to < 1 ml and the post-resection bleeding times was 25 s. Bleeding time, blood loss and the volume of sealant used in the rabbit model were inversely correlated with the thrombin concentration in the sealant. In direct comparisons with Tissucol and Beriplast, Quixil was associated with the shortest bleeding times, the lowest volume of sealant used and the lowest score of abdominal adhesions.

Use of fibrin sealant as a hemostatic agent after liver biopsy in swine.

Authors: Paulson EK, Stephenson GR, Neal MC, Rossin V, Lawson JH

Publication Date: 2000

Abstract:

PURPOSE: To determine whether fibrin sealant injected into the tract created by liver biopsy can be used to decrease postprocedural bleeding. An innovative delivery system was used to deploy the fibrin sealant.

MATERIALS AND METHODS: Fibrin sealant is a hemostatic agent consisting of a suspension of fibrinogen and thrombin. A delivery system was devised whereby fibrin sealant could be injected into the tract created by liver biopsy. Thirty swine were randomized into three groups: control (n = 10), heparin (n = 10), and warfarin (n = 10). Each swine underwent laparotomy and was randomized to undergo three to five open liver biopsies with either a 14-gauge cutting needle in conjunction with the fibrin sealant device or a standard 14-gauge cutting needle alone. Forty-seven biopsy procedures were performed with the device; 64 biopsy procedures were performed without the device. Immediate blood loss per biopsy (mL) was estimated based on the size of the blood stain on a sponge. Specimens were assessed for sample size.

RESULTS: Immediate blood loss with and without the device, respectively, was: control, 0.1 mL, 5.4 mL; heparin, 0 mL, 7 mL; warfarin, 0.1 mL, 9.3 mL. These differences were significant ($P < .01$) for each group of swine. In 43 of 47 biopsies (91%), the device functioned without difficulty. There was no difference in sample size when the device was used.

CONCLUSIONS: The fibrin sealant device is effective in reducing bleeding after open liver biopsy in

anticoagulated and nonanticoagulated swine. The promising results suggest that a trial of percutaneous liver biopsy in swine should be considered.

Hemostatic efficacy of fibrin sealant (human) on expanded poly-tetrafluoroethylene carotid patch angioplasty: a randomized clinical trial.

Authors: Jackson MR, Gillespie DL, Longenecker EG, Goff JM, Fiala LA, O'Donnell SD, Gomperts ED, Navalta LA, Hestlow T, Alving BM

Publication Date: 1999

Abstract:

PURPOSE: The efficacy of solvent-detergent-treated fibrin sealant (human [FSH]) for controlling anastomotic bleeding from expanded polytetrafluoroethylene (ePTFE) patch angioplasty during carotid endarterectomy was evaluated, and FSH was compared with thrombin-soaked gelatin sponge (Gelfoam; TSG).

METHODS: The study was of a randomized, open-label, single-site, single-treatment, parallel design that took place in a referral center with hospitalized patients. Forty-seven adult patients (33 men, 14 women) underwent elective carotid endarterectomy. Patients were randomized to receive either FSH (N = 24) or TSG (N = 23). FSH was obtained as an investigational new drug. FSH was applied as a liquid by means of a dual-syringe technique. Heparin anticoagulation, patch thickness, and suture type were standardized. Two different needle sizes were used (CV-6, PT-13: N = 21 [FSH: N = 10, TSG: N = 11]; CV-6, PT-9: N = 26 [FSH: N = 14, TSG: N = 13]). The FSH or TSG was applied to the ePTFE patch, and then blood flow was restored through the carotid artery. Degree of anticoagulation was assessed by anti-factor Xa activity. The time from restoration of carotid blood flow until achieving hemostasis was recorded. The blood loss from patch suture hole bleeding was measured. Completion intraoperative duplex ultrasound scanning was performed in all cases. Heparin was reversed with protamine sulfate. The primary end point was successful hemostasis

within 15 minutes of restoration of carotid blood flow. The secondary end points were the amount of blood loss caused by suture line bleeding and the time to achieve hemostasis.

RESULTS: There was no difference in the number of patients with complete hemostasis at 15 minutes (TSG, 13 of 23; FSH, 12 of 24; P =.77). The measured blood loss was 99.0 +/- 119.9 (SD) mL for TSG, and 105.0 +/- 107.9 mL for FSH (P =.86). The time to hemostasis was the same for both groups (TSG, 16.5 +/- 16.5 minutes; FSH, 16.6 +/- 14.2 minutes; P =.97). Within both treatment groups, the use of larger needles (PT-13) was associated with greater blood loss (FSH, 169.7 +/- 124.2 mL; TSG, 172.7 +/- 151.5 mL) than was the use of smaller needles (PT-9; FSH, 58.8 +/- 66.3 mL; TSG, 34.1 +/- 25.6 mL; P =.036, P =.001, respectively). There were no postoperative strokes or bleeding complications in either group. No abnormalities were shown in either group by means of completion carotid duplex ultrasound scanning.

CONCLUSION: FSH was equivalent, but not superior to, TSG in achieving hemostasis during carotid endarterectomy performed with ePTFE patch angioplasty. Adhesion properties of FSH to ePTFE are possibly different than those to native tissue and warrant additional investigation.

Reduction of femoral artery bleeding post catheterization using a collagen enhanced fibrin sealant.

Authors: Falstrom JK, Goodman NC, Ates G, Abbott RD, Powers ER, Spotnitz WD

Publication Date: 1997

Abstract:

As the number of cardiac catheterization procedures increases, so do associated complications and costs. This study suggests that the application of a new collagen enhanced fibrin sealant, Collaseal, may be used effectively to achieve rapid hemostasis at the arterial puncture site following femoral artery catheterization. Results in nine dogs anticoagulated with heparin (activated clotting time 396 +/- 107, mean +/- S.D.) revealed a statistically significant reduction in signs of gross bleeding in the sealant-treated groins as compared to control (2 versus 9, P = .0156). These results indicate that this commercially produced sealant might be used in human patients undergoing cardiac catheterization to decrease complications, lengths of stay, and costs.

Reduction of femoral arterial bleeding post catheterization using percutaneous application of fibrin sealant.

Authors: Ismail S, Combs MJ, Goodman NC, Teotia SS, Teates CD, Abbott RD, Fechner RE, Nolan SP, Powers ER, Spotnitz WD

Publication Date: 1995

Abstract:

The number of cardiac catheterizations performed yearly is growing with correspondingly increasing amounts of morbidity, complications, and hospital costs. This study suggests that fibrin sealant instillation via an arterial sheath at the completion of femoral catheterization may improve hemostasis. Results using fibrin sealant in 12 unheparinized dogs documented significant reductions (McNemar's exact test) versus control for groin ecchymoses (1 versus 8, P = .008) and radiolabeled hematoma formation (0 versus 7, P = .016). Also swelling was less in the fibrin sealant treated groins when compared to control groins (1 versus 6, P = .125), but failed to reach statistical significance. Results in eight heparinized dogs (activated clotting time 374 +/- 22, mean +/- SEM) revealed a statistically significant reduction in signs of gross bleeding in the fibrin sealant-treated groins (1 versus 8, P = .016). This method may contribute to reduced morbidity, complications, and length of hospitalization. It may also allow for earlier patient mobilization after cardiac catheterization.

Prevention of bleeding after endoscopic submucosal dissection for gastric neoplasms using polyglycolic acid sheets and fibrin glue.

Authors: Tsuji Y., Fujishiro M., Kataoka Y., Saito I., Shichijo S., Sakaguchi Y., Yamaguchi D., Niimi K., Ono S., Kodashima S., Yamamichi N., Koike K.

Publication Date: 2015

Abstract:

Introduction: For bleeding after endoscopic submucosal dissection (ESD) for gastric neoplasms, no preventive method has been established other than preventive coagulation of visible vessels on the artificial ulcer after ESD or the usage of proton pump inhibitors. We have reported that the endoscopic tissue shielding method with polyglycolic acid (PGA) sheets and fibrin glue can reduce the risk of post-ESD bleeding. Aims & Methods: The aim of this study is to evaluate the efficacy of PGA sheets and fibrin glue for preventing bleeding after gastric ESD after accumulating more cases. This is a non-randomized historical controlled study. We defined high-risk patients for post-ESD bleeding as follows: 1) those who took antithrombotic drugs regularly; or 2) those expected to undergo large mucosal resection (>=40mm). We enrolled patients scheduled to undergo gastric ESD and had above-mentioned risk factors from July 2013 as the study group (Group A). Immediately after ESD we placed PGA sheets on the mucosal defect and fixed them with fibrin glue in the study group. We extracted high-risk patients from those who had undergone gastric ESD at our institution before the enrollment of the first study patient, and defined the group as the historical control group (Group B). The post-ESD bleeding rate was the primary endpoint in comparative analysis. Results: From July 2013 to October 2014, 98 ESD-induced ulcers in 91 high-risk patients were enrolled in Group A. In Group B, 91 ESD-induced ulcers in 84 consecutive patients were extracted between January 2012 and July 2013. There was a significant difference in antithrombotic drugs use (A: 62 lesions, 63.3%, B: 44, 48.4%; P = 0.039), but the other baseline characteristics

were not significantly different between the two groups: sex (A: male 86/female 12, B: male 73/female 18; P = 0.156); age (A: 71.8+/-8.2 yrs, B: 73.3+/-7.9 yrs; P = 0.229); Heparin bridging therapy (A: 18 lesions, 18.4%, B: 10, 11.0%; P = 0.151); and the diameter of resected specimens (A: 43.7+/-16.1 mm, B: 48.1+/-19.7 mm; P = 0.094). Perforation did not occur in either group. Post-ESD bleeding occurred in 7.1% of the study group (7 lesions), and 17.6% of the historical control group (16 lesions). There was a significant difference in the post-ESD bleeding rate between the two groups (P = 0.027). Multivariate logistic regression analysis also confirmed that applying PGA sheets and fibrin glue was an independent significant factor for decreasing the risk of post-ESD bleeding (Odds Ratio, 0.33; 95% CI: 0.11-0.89, P = 0.029). The mean procedural time for applying PGA sheets and fibrin glue was 20.0+/-9.1 min. Conclusion: Even after accumulating more cases, this study all the same implied that the endoscopic tissue shielding method with PGA sheets and fibrin glue might be promising for the prevention of post-ESD bleeding.

Prevention of bleeding after endoscopic submucosal dissection for gastric neoplasms using polyglycolic acid sheets and fibrin glue.

Authors: Tsuji Y., Fujishiro M., Kataoka Y., Saito I., Sakaguchi Y., Minatsuki C., Hirayama I., Niimi K., Ono S., Kodashima S., Yamamichi N., Koike K.

Publication Date: 2015

Abstract:

Background: For bleeding after endoscopic submucosal dissection (ESD) for gastric neoplasms, no preventive method has been established other than preventive coagulation of visible vessels on the artificial ulcer after ESD or the usage of proton pump inhibitors. We have reported that the endoscopic tissue shielding method with polyglycolic acid (PGA) sheets and fibrin glue can reduce the risk of post-ESD bleeding. Aim: To evaluate the efficacy of PGA sheets and fibrin glue for preventing bleeding after gastric ESD after accumulating more cases. Methods: This is a non-randomized historical controlled study. We defined high-risk patients for post-ESD bleeding as follows: 1) those who took antithrombotic drugs regularly; or 2) those expected to undergo large mucosal resection (>= 40mm). We enrolled patients scheduled to undergo gastric ESD and had above-mentioned risk factors from July 2013 as the study group (Group A). Immediately after ESD we placed PGA sheets on the mucosal defect and fixed them with fibrin glue in the study group. We extracted high-risk patients from those who had undergone gastric ESD at our institution before the enrollment of the first study patient, and defined the group as the historical control group (Group B). The post-ESD bleeding rate was the primary endpoint in comparative analysis. Results: From July 2013 to October 2014, 98 ESD-induced ulcers in 91 high-risk patients were enrolled in Group A. In Group B, 91 ESD-induced ulcers in 84 consecutive patients were extracted between January 2012 and July 2013. There was a significant difference in antithrombotic drugs use (A: 62 lesions, 63.3%, B: 44, 48.4%; P = 0.039), but the other baseline characteristics were not significantly different

between the two groups: sex (A: male 86/female 12, B: male 73/female 18; P = 0.156); age (A: 71.8 +/- 8.2 yrs, B: 73.3 +/- 7.9 yrs; P = 0.229); Heparin bridging therapy (A: 18 lesions, 18.4%, B: 10, 11.0%; P = 0.151); and the diameter of resected specimens (A: 43.7 +/- 16.1 mm, B: 48.1 +/- 19.7 mm; P = 0.094). Perforation did not occur in either group. Post-ESD bleeding occurred in 7.1% of the study group (7 lesions), and 17.6% of the historical control group (16 lesions). There was a significant difference in the post-ESD bleeding rate between the two groups (P = 0.027). Multivariate logistic regression analysis also confirmed that applying PGA sheets and fibrin glue was an independent significant factor for decreasing the risk of post-ESD bleeding (Odds Ratio, 0.33; 95% CI: 0.11-0.89, P = 0.029). The mean procedural time for applying PGA sheets and fibrin glue was 20.0 +/- 9.1 min. Conclusion: Even after accumulating more cases, this study all the same implied that the endoscopic tissue shielding method with PGA sheets and fibrin glue might be promising for the prevention of post-ESD bleeding.

Endoscopic tissue shielding method with polyglycolic acid sheets and fibrin glue decreases the risk of bleeding after endoscopic submucosal dissection of gastric neoplasms.

Authors: Tsuji Y., Fujishiro M., Sakaguchi Y., Minatsuki C., Asada-Hirayama I., Niimi K., Mochizuki S., Ono S., Kosdashima S., Yamamichi N., Koike K.

Publication Date: 2014

Abstract:

INTRODUCTION: Prevention of bleeding after endoscopic submucosal dissection (ESD) for gastric neoplasms is still an important problem, but there have been no preventive measures other than proton pump inhibitor use and preventive coagulation of visible vessels on the artificial ulcer after ESD. AIMS & METHODS: We aimed to evaluate the efficacy and safety of the tissue shielding method with polyglycolic acid (PGA) sheets and fibrin glue for preventing bleeding after gastric ESD. This is a non-randomized historical controlled study. We defined high-risk patients for post-ESD bleeding as follows: 1) those who took antithrombotic drugs regularly; or 2) those who were expected to undergo large mucosal resection (>= 40mm). We enrolled patients who were scheduled to undergo gastric ESD and had above-mentioned risk factors from July 2013 as the study group (Group A). We placed PGA sheets on the mucosal defect and fixed with fibrin glue in the study group. Between January and July 2013, before the first enrolment of a study patient, 126 gastric neoplasms in 101 consecutive patients were treated with ESD. From this cohort, we extracted high-risk patients as the historical control group (Group B). We set the post-ESD bleeding rate as the primary endpoint to compare both groups. RESULTS: From July 2013 to February 2014, 45 ESD-induced ulcers in 41 highrisk patients for bleeding were enrolled in the study group. In the historical control group, 41 ESD-induced ulcers in 37 patients were extracted. The baseline characteristics were not significantly different between the two groups: sex (A: male 41/female 4, B:

male 34/female 7; P = 0.256); age (A: 73.6 +/- 7.5 yrs, B: 74.8 +/- 7.0 yrs; P = 0.482); antithrombotic drug use (A: 29 lesions, 66.4%, B: 23 lesions, 56.1%; P = 0.429); Heparin bridging therapy (A: 7 lesions, 15.6%, B: 3 lesions, 7.3%; P = 0.319); and the diameter of resected specimens (A: 40.1 +/- 12.4 mm, B: 43.9 +/- 15.1 mm; P = 0.206). Neither intraoperative perforation or delayed perforation occurred in the two groups. Post-ESD bleeding occurred at a rate of 6.7% in the study group (3 lesions), and 22.0% in the historical control group (9 lesions). There was a significant difference in the post-ESD bleeding rate between the two groups (P = 0.041). In the study group, post-ESD bleeding occurred only in heparin bridging therapy. In the study group, the procedural time for applying PGA sheets and fibrin glue was 20.4 +/- 9.5 min. CONCLUSION: The endoscopic tissue shielding method with PGA sheets and fibrin glue appears to be promising for the prevention of post-ESD bleeding.

Intraoperative haemostasis with new fibrin surgical sealant Quixil in gynaecological oncology.

Authors: Papacharalabous E.N., Giannopoulos T., Tailor A., Butler-Manuel S.A.

Publication Date: 2009

Abstract:

We evaluated the effectiveness and safety of Quixil in gynaecological oncology with a prospective observational study over 11 months in a gynaecological oncology centre. Quixil was opportunistically used when conventional haemostatic techniques failed, in 35 laparotomies and four laparoscopies. A total of 26 operations were performed for malignant disease and 13 for benign indications. Demographic, intraoperative and postoperative data were collected. Haemostasis was accomplished within 5 min from sealant application. No hypersensitivity reactions were noted. Bowel recovery and postoperative pain were usual. In the laparotomy group, the mean hospital stay was 11 days and mean operating time, 164 min. In the laparoscopy group, the mean hospital stay was 3 days and mean operating time 165 min. In both groups, the incidence of complications and recurrence rates were in line with the expected population rates of these treated patients. We conclude that Quixil is an efficient, safe and effective haemostatic agent, which has a role to play in gynaecological surgery for benign and malignant disease.

Hemostatic effectiveness of a new application method for fibrin glue, the "rub-and-spray method", in emergency aortic surgery for acute aortic dissection.

Authors: Minato N., Katayama Y., Yunoki J., Kawasaki H., Satou H.

Publication Date: 2009

Abstract:

Purpose: This study was performed to evaluate the clinical hemostatic effectiveness of a new application method for fibrin glue, the rub-and-spray method, in aortic surgery. Methods: Twenty consecutive patients undergoing emergency ascending aorta or ascending- hemiarch replacement for Stanford type A acute aortic dissection were prospectively randomized into 2 groups, one with the rub-and-spray method (group G, 10 patients) and one without fibrin glue (group C, 10 patients). The rub-and-spray method consists of using a finger to rub the fibrinogen solution over needle holes, then spraying the fibrinogen solution and the thrombin solution simultaneously over the anastomosis, using an application nozzle. The number of bleeding needle holes at the proximal and distal anastomoses just after reperfusion, the hemostatic period (time from administration of protamine sulfate until closure of the pericardium), and the amounts of blood losses during this hemostatic period were measured. Results: The values in group G and group C were as follows: proximal needle holes (26.8 +/- 1.5, 26.4 +/- 2.4, p = 0.466); proximal bleeding needle holes (0.2 +/- 0.4, 19.3 +/- 3.5, p <0.001); distal needle holes (28.7 +/- 2.5, 27.8 +/- 4.4, p = 0.675); distal bleeding needle holes (1.3 +/- 1.2, 19.9 +/- 5.0, p <0.001); estimated bleeding proportion of the proximal needle holes (0.7 +/- 1.6%, 73.8 +/- 16.0%, p <0.001); estimated bleeding proportion of the distal needle holes (4.4 +/- 3.7%, 71.9 +/- 15.7%, p <0.001); estimated median hemostatic period (41.5 min [32-49], 51 min [44-89], p = 0.036); amounts of blood losses during this hemostatic period (99 +/- 76 ml, 257 +/- 163 ml, p = 0.016). The number of bleeding needle holes, the bleeding proportion

of the proximal and distal needle holes, the hemostatic period, and the amounts of bleeding during this hemostatic period were significantly less in group G. Conclusion: This new application method for fibrin glue, the rub-and-spray method, revealed significant hemostatic effectiveness, even in hemostatically difficult surgery of acute aortic dissection that requires systemic heparinization and prolonged cardiopulmonary bypass with deep hypothermia.