Acute Occlusion of the Superior Mesenteric Artery

Diagnosis and treatment

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Abstract

Acute occlusion of the superior mesenteric artery (SMA) is a condition associated with high mortality and morbidity. The aim of this thesis is to evaluate diagnostic and therapeutic approaches for acute SMA occlusion.

In a prospective study of patients with suspected intestinal ischemia, no biomarker was sufficiently accurate to detect this condition. In a second retrospective study, pancreatic amylase and troponin-I were elevated in a substantial proportion of patients with verified SMA occlusion.

In an experimental animal model of acute SMA occlusion, microarray studies of ischemic small bowel wall were used to characterize the mRNA response to ischemia. Thrombospondin, Monocyte Chemoattractant Protein 1 and Gap Junction Alpha 1 were consistently up-regulated in all pigs with intestinal ischemia. Genes encoding previously proposed biomarkers for intestinal ischemia were either up-regulated, such as lactate dehydrogenase and creatine kinase, or down-regulated, such as intestinal fatty acid binding protein and glutathione S-transferase.

In a study of the role of computed tomography in the diagnosis of SMA occlusion, it was shown that computed tomography with intravenous contrast was associated with improved survival.

A retrospective analysis of all acute SMA revascularizations in Sweden 1999-2006 revealed that D-dimer was elevated in all 35 measured cases. Endovascular surgery was associated with better outcome than open surgery, both in short and in long term. The presence of postoperative short bowel syndrome was a strong independent risk-factor for decreased long-term survival.

Conclusions: Data affirm that D-dimer may serve as an exclusion test for acute SMA occlusion, whereas elevated troponin-I and pancreatic amylase are potential diagnostic pitfalls. Contrast-enhanced computed tomography of the visceral arteries seems to be the best diagnostic method. Endovascular surgery is an option to open surgery in selected cases, and was associated with favourable outcome.

Keywords: superior mesenteric artery, acute mesenteric ischemia, acute thrombo-embolic occlusion, computed tomography, vascular surgery, serum biomarkers, microarray, intestinal revascularization

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“The diagnosis impossible, the treatment useless, and the prognosis almost hopeless…”

AJ Cokkinis
on SMA occlusion 1926
List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.


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Abbreviations

AAA  Abdominal Aortic Aneurysm
ACS  Abdominal Compartment Syndrome
AF  Atrial Fibrillation
AMI  Acute Mesenteric Ischemia
APP  Abdominal Perfusion Pressure
CA  Celiac artery
CI  Confidence Interval
CRP  C-reactive Protein
CT  Computed Tomography
CTA  Computed Tomography Angiography
CVD  CerebroVascular Disease
IAH  Intra-Abdominal Hypertension
IHD  Ischemic Heart Disease
IMA  Inferior Mesenteric Artery
IQR  Inter Quartile Range
LR  Likelihood Ratio
MDCTA  Multi Detector Computed Tomography Angiography
mRNA  Messenger Ribonucleic Acid
MRT  Magnetic Resonance Tomography
MUH  Malmö University Hospital
OECD  Organization for Economic Co-operation and Development
rAAA  Ruptured Abdominal Aortic Aneurysm
SMA  Superior Mesenteric Artery
SWEDVASC  The Swedish Vascular Registry
TnI  Troponin-I
WBC  White Blood Cell count
WSACS  World Society for the Abdominal Compartment Syndrome
Introduction

Definition
Mesenteric ischemia is defined as an inadequate delivery of oxygen to the cells of the mesentery, i.e. the gastrointestinal tract from the stomach to the anus, including the small intestine, colon, pancreas, liver and gallbladder. If a particular vessel is involved, the anatomical location determines what organ that will be affected. Mesenteric ischemia can be chronic or acute and in some cases acute superimposed on chronic. It can be due to general hypoxia, bowel strangulation, arterial or venous occlusion and non-occlusive hypoperfusion. This thesis is focused on acute mesenteric ischemia due to occlusion of the superior mesenteric artery (SMA).

History of mesenteric ischemia
The first description of mesenteric ischemia was made by Antonio Bienvenie, who lived in 15th century Florence. The first successfully treated case was reported in 1895, by Elliott who performed intestinal resection and anastomosis in a patient with acute mesenteric ischemia (AMI). Even early in the history of AMI, the condition was recognized as one with dismal prognosis, as noted by Cokkinis in 1926. Klass performed the first superior mesenteric artery embolectomy in 1950, preventing intestinal resection (Klass). Thrombectomy of the SMA was described in 1958 by Shaw and Maynard (Shaw). Furrer et al performed the first percutaneous angioplasty of the SMA in 1980 (Furrer), pioneering endovascular surgery for mesenteric vascular disease.

Anatomy and physiology
During fasting conditions, 20-25% of the total arterial circulation is distributed to the three major splanchnic arteries; the celiac artery (CA), the superior mesenteric artery (SMA) and the inferior mesenteric artery (IMA). The splanchnic arteries receive approximately 800 ml (CA), 500 ml (SMA) and 50 ml (IMA) blood/minute, respectively (Kolkman 2003).

The arterial branches first reach the serosal layer of the gut, then the muscular layer, and finally terminate in the mucosal branches. In the presence of hypotension, local vasodilation ensures adequate perfusion
within a wide pressure range (Bulkley 1987). Two other mechanisms to ensure oxygen supply is increased oxygen extraction and internal intestinal redistribution of blood flow to the metabolically more demanding mucosa (Haglund 1999).

The CA arises from the aorta in a nearly perpendicular angle (figure 1), just below the diaphragm, and supplies the stomach, the duodenum, the spleen and the liver through the left and right gastric arteries, the gastroduodenal artery, the hepatic artery and the splenic artery, respectively. The organs supplied by the CA have an interdependent collateral blood flow making them less vulnerable to peripheral arterial occlusion. The CA and SMA share a collateral blood flow, with great individual differences, through the superior and inferior pancreaticoduodenal arteries.

Figure 1. Anatomy of the mesenteric arterial circulation

The SMA arises from the aorta in an oblique angle behind the pancreas, supplying the jejunum, ileum as well as the ascending and transverse colon
The marginal artery of Drummond, running in the mesentery alongside the colon, is supplied by both the SMA and IMA and constitutes a collateral circulation for the large intestine. The meandering mesenteric artery, also called the Arcade of Riolan, is a collateral vessel important in chronic pathologic redistribution of mesenteric arterial circulation (Gourley). This collateral vessel connects the middle and left colic artery and runs in a tortuous fashion in the left upper quadrant of the abdomen. The artery of Drummond and the meandering mesenteric artery can attenuate ischemia in the small or large intestine caused by isolated peripheral occlusion of the SMA or IMA. However, there is little if any collateral circulation to the small intestine in a healthy person, leaving this organ highly vulnerable to acute arterial occlusion of the SMA.

The IMA arises from the mid section of the abdominal aorta and supplies the descending colon, the sigmoideum and the proximal part of the rectum. As mentioned above, IMA and SMA share a collateral blood flow through the meandering mesenteric artery. There is also a collateral blood flow from the left internal iliac artery for the tissues supplied by the IMA, as well as a rich collateral blood-flow between the left and right internal iliac arteries.

**Pathophysiology**

Due to the metabolic and anatomical conditions mentioned above, the mucosal layer is the most susceptible to intestinal ischemia. In response to ischemia, the intestine responds by basal shunting of the circulation to the base of the villi in order to minimize oxygen consumption and preserve bowel integrity (Haglund 1987). As a consequence, in ischemic conditions, the mucosal layer is sacrificed first in order to preserve bowel integrity. The intestinal tissue responds to ischemia by arteriolar smooth muscle relaxation and metabolic response. If the blood flow decreases below 30ml/100g tissue, oxygen consumption drops markedly in order to prevent necrosis (Bulkley 1985). Hypovolemia in the patient with acute occlusive ischemia can further exacerbate oxygen delivery by activation of the renin-angiotensin axis (Reilly) and thus promoting vasoconstriction of the mesenteric arterial circulation.

If ischemia prevails, development of transmural infarction occurs and eventually, bowel wall integrity is compromised. If untreated, this leads to peritonitis, septic shock and death.
Pathogenesis

Arterial embolism to the SMA
Due to the oblique angle of the SMA relative to the aorta, the SMA is susceptible to arterial embolism which is most commonly dislodged in the proximal part of the SMA, sparing the jejunal branches (Bergan 1967). The sources of emboli are often of cardiac origin due to infarction, atrial fibrillation, cardiac thrombus or cardiac valvular disease. In this group of patients, there are rarely signs of previous abdominal angina and the onset of pain and symptoms is sudden. There may be other manifestations of arterial embolic disease such as a previous history of ischemic stroke and/or emboli to other organs. Synchronous emboli are present in 2/3 of the patients (Acosta 2005). Embolism can also be secondary to aortic thrombus, arterial catheterization, or paradoxical venous thromboembolism through a patent foramen ovale.

Arterial thrombosis of the SMA
Patients with arterial thrombosis of the SMA share the common features associated with atherosclerotic disease such as hypertension, hyperlipidemia, diabetes and smoking. They often present with a previous history of myocardial infarction and/or stroke (Järvinen, Björck 2002). There may be symptoms of previous abdominal angina with diarrhoea, post-prandial pain and involuntary weight loss. The thrombosis often occurs in an area with turbulent flow, i.e. the proximal SMA, or in the ostial SMA due to calcification of the aorta. In thrombotic occlusions, several SMA branches may be occluded, but the extent of infarction is dependent on collateral circulation and possibly hypoxic preconditioning (Mallick).

Other causes of arterial SMA occlusion
Dissection of the aorta can cause occlusion of the SMA and subsequent mesenteric ischemia. This can be treated with intra-aortic fenestration, endovascular surgery or open surgery (Sandridge). Isolated spontaneous dissection of the SMA is a rare condition and the mainstay of treatment is expectancy, possibly anticoagulation therapy and conservative approach to invasive treatment (Yun). Iatrogenic dissection can occur during open or endovascular surgery and should be treated promptly (Dias). With increasing numbers of endovascular stent procedures on the SMA, there have been documented cases of stent thrombosis, causing acute SMA occlusion (Dias).
Epidemiology

Incidence

There is only one population-based study of the epidemiology of acute occlusive mesenteric disease (Acosta 2004 EJVES). The reported incidence of SMA occlusion in the population of Malmö, based on an 87% autopsy rate combined with clinical data, was 8.6/100000 person-years. In relation to this, ruptured abdominal aortic aneurysm had an incidence of 5.6/100000 in the same population. The incidence increases exponentially with age (fig 2) with an incidence rate exceeding 100/100000 in octogenarians. When adjusted for age and gender in the population, acute SMA occlusion is equally common in men and women.

Figure 2. Incidence of acute SMA occlusion related to age (Acosta 2004)

Thrombotic versus embolic occlusion

Thrombotic occlusions account for approximately 2/5 of acute thromboembolic occlusions of the SMA (Acosta 2005). The thrombotic
occlusions, as already mentioned, are often located proximally in the SMA. Consequently, if ischemia occurs, it can be widespread throughout the area of distribution of the SMA. There are often concomitant atherosclerotic changes in the mesenteric vasculature (Acosta 2005) and symptoms of previous chronic mesenteric ischemia are often reported in patients with acute thrombotic occlusion (Acosta 2005).

In embolic patients, acute myocardial infarction, atrial fibrillation and synchronous emboli, are common findings. Synchronous emboli overall are present in 2/3 patients and visceral synchronous embolism is found in 2/5 patients (Acosta 2005). The embolus tends to lodge distally to the first branches, sparing the duodenum and proximal jejunum (Acosta 2005). Previous publications have reported on a higher mortality (Schoots 2004) and more extensive bowel ischemia (Björck 2002, Acosta 2005) in patients with thrombotic versus embolic occlusion.

**Mortality**

Acute arterial occlusion of the SMA has remained a condition with high mortality with earlier studies reporting on mortality rate up to 80-90% (Järvinen, Mamode). Conservative treatment results in a mortality of 100% with rare exceptions. In patients treated with bowel resection only, short-term survival can be achieved in 49% of the cases (Järvinen). Despite advances in surgical and diagnostic management, contemporary reviews report on a short-term mortality rate of 30-60% in patients undergoing revascularization of the SMA (Kassahun, Björck 2002, Schoots 2004, Park), as compared to survival from ruptured abdominal aortic aneurysm (rAAA), which has a 30-day mortality rate of approximately 25% (Mani). A recent report from the Nationwide Inpatient Sample (USA) (Schermerhorn) reported on an in-hospital mortality rate of 30% for AMI undergoing revascularization, but the data from this registry has not been validated. Data on long-term mortality for patients undergoing intestinal revascularization is lacking, but one study reported on a 1-year mortality rate of 60% and a 5-year mortality rate of 67% (Björck 2002).
Diagnosis

The difficulties to make a correct diagnosis of AMI represent a major obstacle to treatment and favourable outcome since the diagnosis of these patients is difficult, even for senior physicians.

Clinical presentation

Approximately 2/3 or more of patients present with an acute onset of pain (Acosta 2003, Björck 2002). Vomiting and/or diarrhoea can be present but is not mandatory. The hallmark sign is severe abdominal pain with little or no palpatory tenderness on examination - “pain out of proportion”. The clinical course of AMI can be divided into three phases (Kaleya, Shaw):

I. Pain out of proportion. Hyperperistalsis.

Since the initial pain is often followed by a period of relative pain relief, there is an obvious risk that this can mislead the clinician, leading to delayed diagnosis and treatment.

In embolic patients, “the clinical triad”, consisting of source of emboli, pain out of proportion and bowel emptying, can be seen in 40-80% of patients with embolic occlusion (Kassahun, Acosta 2003).

Thrombotic occlusions can present with various time range, depending on the presence of previous abdominal angina and collateral circulation (Berland). In contrast, embolic occlusions present with acute onset of symptoms in most, but not all, cases.

Laboratory tests on blood samples

The laboratory findings in these patients display a great variety, depending on pathogenesis, duration of disease and co-morbidity. In late stages, lactate, low pH and a high anion gap all reflect the development of systemic shock in response to the abdominal sepsis. However, in the early clinical course, these variables are most likely normal. Various serum biomarkers, such as
intestinal fatty-acid binding protein, glutathione transferase and D-lactate have been proposed as candidates for detecting AMI, but none have proved accurate enough (Evennett).

D-dimer

D-dimer protein represents the final stage of plasmin-mediated degradation of fibrin, thus indicating ongoing fibrinolysis. Indirectly, it therefore indicates a preceding state of increased fibrin formation. It is a highly unspecific marker for a number of conditions, such as sepsis, trauma, pre eclampsia and various malignancies but the analysis is mainly used in the diagnosis of thromboembolic diseases. In acute SMA occlusion, D-dimer has been used mainly as an exclusion test (Acosta 2004 BJS).

Plain x-ray abdominography

Plain x-ray of the abdomen is completely normal in 1/4 of patients with AMI (Smerud). Nonspecific findings of AMI are signs of ileus, bowel wall oedema, thumbprinting and in advanced cases pneumatosis in the bowel wall or porto-mesenteric venous circulation.

Duplex sonography

Duplex sonography is non-invasive and has been documented as diagnostic for patients with CMI (Moneta). However, the method is highly operator-dependent and therefore not always available on a 24-hour basis. Furthermore, the acute abdomen in a non-fasting patient can make the examination very challenging in patients with SMA occlusion and duplex cannot provide the surgeon with information on distal anatomy and collaterals. This makes the method prone to false negative results, in particular among patients with embolic occlusion, where the embolus typically occludes the SMA distant to the origin of the vessel from the aorta (Björck 2002).

Magnetic resonance tomography

The advantages of magnetic resonance tomography (MRT) include less risk of allergic reactions to iodinated contrast agents compared to computerized tomography and an ability to incorporate functional evaluations of the intestine (Li). However, MRT is time-consuming, not readily available and,
with the patient in the tomography, makes it difficult to pursue resuscitation and/or interventions during the examination. In addition to that, MRT has poorer resolution than computerized tomography (CT) and therefore it is difficult to evaluate the distal mesenteric arteries with this method (Meaney).

Computed tomography angiography

Multi detector row computed tomography angiography (MDCTA) with intravenous contrast enhancement and imaging in the arterial phase, has been described by several authors in the evaluation of acute intestinal ischemia. MDCTA is available at all hours in virtually every hospital in the OECD-countries (Organisation for Economic Co-operation and Development), the examination is fast and has the advantage of providing detailed information of the visceral organs, thereby enabling the radiologist to evaluate not only the mesenteric circulation but also the intestines and exclude any other intra-abdominal pathologies. Kirkpatrick et al demonstrated a sensitivity of 96% and a specificity of 94% for the diagnosis of AMI in 62 prospectively evaluated patients when using biphasic MDCTA. These findings has since then been confirmed by other studies using biphasic MDCTA (Aschoff, Ofer), reporting a sensitivity and specificity of 93% and 100%, and 93% and 99%, respectively. Biphasic MDCTA has the advantage of combining arterial phase imaging for vessels and venous phase to assess possible signs of infarcted intestinal tissue in one contrast dose. In these studies, no single finding was 100% sensitive or specific but when combining different criteria (pneumatosis, bowel wall oedema, portal venous gas etc) accuracy for MDCTA in diagnosing AMI is above 95% (Aschoff, Ofer). In a recent meta-analysis, MDCTA had a pooled sensitivity and specificity of 93.3% and 95.9% respectively (Menke). In this meta-analysis, MDCTA was suggested as the first-line imaging method for AMI.

Figure 3. MDCTA images of an embolic SMA occlusion in sagittal, coronal and axial planes.
Angiography

Angiography has been proposed as the “golden standard” for diagnosing mesenteric vascular occlusion (Boley). Imaging in the anterior and lateral view offers detailed information on the mesenteric vasculature regarding flow dynamics, extent of occlusive disease and collateral circulation. Furthermore, it is a mandatory adjunct to endovascular intervention which is increasing in the management of acute SMA occlusion. Still, many centres do not have access to angiography on a 24-hour basis or do not have access to it at all. This limits the use of angiography as the primary diagnostic method in the emergency setting.

![Figure 4. Anterior and lateral angiography of SMA and distal branches](image)

Diagnostic laparoscopy

Laparoscopy, combined with fluorescein and ultraviolet light has been proposed as a diagnostic method for detecting AMI (Paral). However, there is a risk of missing areas of affected ischemic bowel, due to technical difficulties in exposing the entire intestinal length by laparoscopic method (Sauerland). Furthermore, there is a risk of penetrating nonviable fragile ischemic bowel and thus contaminating the abdominal cavity. Extensive bowel paralysis and bleeding after grabbing the mesentery are other factors that limit the use of laparoscopy for safe inspection of the bowels, even for experienced operators.
Management

Open surgical revascularization

The abdomen is explored through a midline incision from the xiphoid bone to the symphysis pubis. If a bypass or a patch is likely to be needed, the patient should be prepared and draped to the knees bilaterally to allow for harvesting of saphenous vein material and/or endovascular access through the femoral artery. The SMA is exposed by retracting the omentum and transverse colon cephalad and the small bowel and mesentery caudally (Kazmers). Through a horizontal incision in the root of the mesentery of the transverse colon, the SMA can be isolated and controlled. If an embolectomy is indicated, a transverse incision is sufficient but if a bypass or thrombendarterectomy is anticipated, the artery is incised longitudinally.

SMA embolectomy

After incision of the SMA, the proximal SMA is vented and, if necessary, catheterized with a 3 French (Fr) or 4Fr balloon catheter until inflow is established. Distally, a 2Fr or 3 Fr catheter is used with great care to avoid dissection and damage to the intima. Alternatively, the SMA can be “milked” in proximal direction to remove thrombotic material. After retrograde flow is established, an anti-coagulant agent such as heparin can be administered distally into the SMA.

SMA bypass

In thrombotic occlusion, SMA bypass is an alternative to open surgery. Graft orientation and placement is largely dependent on existing intra-abdominal vessels regarding atherosclerosis and anatomy. Retrograde bypass, using one of the common iliac arteries as inflow, avoids clamping the aorta, a procedure that can be detrimental in these fragile patients. Furthermore, it is common that the aorta is heavily calcified, making by-pass from the aorta impossible without simultaneous thrombendarterectomy, making it a major procedure. Antegrade by-pass is more time-consuming but is an alternative for elective operation on patients with chronic mesenteric ischemia (Oderich 2010). The choice between autologous vein material and a prosthetic graft is influenced by the presence or absence of peritoneal contamination and the
risk of kinking. Prosthetic grafts have the advantage of being less prone to kinking and external compression and require less operative time, which may be decisive in these critically ill patients. Division of the SMA with re-implantation into the infra-renal aorta or local thrombendarterectomy are other surgical options. A patient with AMI is preferably treated according to the principles of Damage Control, with abbreviated laparotomy (Rotondo).

Endovascular treatment
Access to the arteries can be made by the femoral, brachial or directly through the superior mesenteric artery via open surgery. The brachial approach is preferred in cases of a highly oblique angle of the SMA or a proximal stenotic lesion, both making the femoral access technically difficult (Resch). After catheterization of the SMA, glucagone is injected intravenously to stop bowel movements for better radiological imaging and heparin is administered. Arterial anatomy is evaluated in both anterior and lateral views, using injection of iodinated contrast.

Aspiration embolectomy
Aspiration embolectomy can be employed in the case of an SMA embolus (Ogihara). In cases of an incomplete embolectomy and/or distal embolization, intra-arterial local thrombolysis with recombinant tissue plasminogen activator can be used as an adjunct to complete lysis. The decision to use thrombolysis must be made with caution, as there may be a risk of severe gastrointestinal bleeding.

SMA stenting
Stenting of the SMA is an alternative in treating thrombotic occlusion. Balloon-expandable stents are used to treat stiff ostial lesions. Self-expandable stents are better used as distal extensions, achieving a smoother transition between the balloon-expandable stent and the native SMA (Resch). Intravascular access can vary, as stated above. In cases where antegrade access is impossible, retrograde access to the SMA can be achieved through laparotomy. Stenting can subsequently be made retrograde or antegrade, by snaring the retrograde inserted guide wire in the aorta from the brachial or femoral artery, creating through and through access. The rationale for this is that antegrade stenting is technically less challenging and can be made using standard techniques and devices (Resch). Retrograde open mesenteric stenting (ROMS) has been described to markedly reduce mortality in small series of patients (Milner, Wyers).
Thrombolysis

Thrombolysis has been described as a stand-alone treatment for acute SMA occlusion, with good outcome (Schoots 2005) but is relatively rare. In a recent publication, thrombolysis has been described as a useful adjunct to endovascular embolectomy (Resch, Acosta 2009) in order to remove residual clotting, as previously described.

Pharmacological management

Vasoactive agents

Papaverine is a non-selective vasodilator agent that inhibits phosphodiesterase, resulting in increased levels of intra-cellular cAMP which results in smooth muscle relaxation. Local intra-arterial administration of papaverine into the SMA for treating AMI has can restore SMA blood flow in an animal model (MacCannell) and is also associated with decreased mortality in patients with AMI (Boley). However, papaverine has also been reported to produce a “steal” phenomenon in a canine model (Bulkley) with dilation of non-ischemic intestinal segments, thus reducing flow in the ischemic segments. There are no randomized trials evaluating the effect of papaverine to standard surgical treatment in acute mesenteric occlusive disease.

Glucagone is an endogenous hormone, causing mesenteric and systemic vasodilation, increased cardiac inotropy and gluconeogenesis. Animal studies have shown a reduction in mortality with administration of glucagon (Gangadhara) in the reperfusion phase but other studies have shown an increase in the reperfusion injury (Clark) when glucagon was administered before revascularization, possibly due to increased metabolism.

Norepinephrine is an endogenous catecholamine with mainly α-adrenergic effects but also β-adrenergic effect. It is recommended as the vasopressor of choice in septic shock (Dellinger), increasing microcirculation in the septic patient due to an increase in mean arterial pressure (MAP). In animal models with induced sepsis and faecal peritonitis, norepinephrine has been shown to increase MAP and thus maintaining mesenteric blood flow (Giantomasso) and preventing gut hyperpermeability (Levy). In a comparison between norepinephrine and dopamine in patients with vasoplegic shock, the ratio of hepatosplanchnic blood flow relative to cardiac output was higher and hepatic lactate-pyruvate ratio was lower with norepinephrine (Guerin).

Dobutamine is a mainly β-adrenergic catecholamine with inotropic and chronotropic effects. It is the drug of choice for treating cardiogenic stunning in septic shock (Dellinger). In an animal model of induced endotoxin shock (Lobo), dobutamine compared to saline increased SMA and aortic blood
flow and decreased ileac mucosal-arterial pCO2-gap, whereas Björck and co-workers did not find an effect of dobutamine on regional SMA blood flow in an animal model for colonic ischemia based on partial SMA occlusion and IMA ligation (Björck 1998).

When comparing norepinephrine, norepinephrine/dobutamine and norepinephrine/dopamine in an animal model for faecal peritonitis (Sun), mesenteric blood flow, reduction of intestinal oedema and animal survival were all favoured by animals treated with norepinephrine/dobutamine.

Vasopressin is recommended as complementary therapy for vasoplegic shock with inadequate response to norepinephrine. Vasopressin has detrimental effects on mesenteric circulation in animals and humans (Martikainen 2003). Dobutamine has been suggested to reverse this adverse effect of vasopressin in septic animal model (Martikainen 2004) but this was disputed by a recent publication (Holt).

Epinephrine is a potent catecholamine with both α- and β-adrenergic stimulation, resulting in tachycardia and marked vasoconstriction. In a porcine model of septic shock, Martikainen and co-workers reported 2005 on decreased portal venous flow, increased venous lactate-pyruvate ratio and induction of intra-peritoneal lactate, all of which could not be seen in subjects treated with norepinephrine.

Levosimendan is a pyridazinone-dinitrile, a calcium-channel sensititizer that promotes cardiac inotropy and vasodilation without increasing oxygen demand. While primarily used in severe congestive heart failure, there are experimental studies on mesenteric circulation. In un-manipulated dogs, levosimendan displayed selectively improved gastric microcirculation without an increase in oxygen demand compared to dobutamine (Schwarte). However, in a study with septic, volume-resuscitated piglets in combination with norepinephrine, dobutamine and levosimendan had similar effect on MAP and systemic oxygen delivery but dobutamine was associated with increased portal blood flow and lower arterial, venous and portal lactate concentrations (Cunha-Goncalves).

Dopexamine is a synthetic dopamine with vasodilatory effects in the splanchnic circulation (Lisbon). In controlled SMA hypoperfusion of 30 mm Hg, dopexamine increased mesenteric oxygen delivery but paradoxically increased mesenteric lactate production while decreasing intra-mucosal pH (Fröjse).

**Bowel assessment and surgery**

Bowel surgery should always, if possible, be postponed until evaluation of the revascularization has been made. After revascularization, reperfusion should be allowed for approximately 30 minutes until the bowel is reassessed (Kazmers). Evaluation of the viability of the intestine is judicious
and involves visible and palpable pulsations in the mesenteric arteries, discoloration, peristalsis and bleeding from cut surfaces. These criteria have been reported to result in a sensitivity of 82% and specificity of 91% in determining bowel viability (Bulkley). Other methods of controlling bowel perfusion include Doppler ultrasound (Hobson), fluorescein fluorometry (Bergman), transit-time flow meter (Björck 2006), duplex ultrasound (Oderich 2003) and laser doppler flow meter (Redaelli).

In a prospective controlled study on patients with ischemic bowel segments, Bulkley and co-workers demonstrated that a fluorescein fluorometry technique had an accuracy of 100% compared to 89% and 84% for standard clinical judgment and Doppler technique, respectively. Doppler and clinical judgment would in this study have led to a high rate (46%) of unnecessary bowel resection.

Second-look surgery
Ultimately, the assessment of bowel viability may not be conclusive during the primary procedure. In this case, a second look operation is planned at a defined time interval. Many surgeons claim a second-look to be mandatory, but there are no data comparing outcome after routine and on-demand re-laparotomy.

On second-look laparotomy, the intestine has more likely demarcated between viable and non-viable segments and bowel resection, if necessary, can be made with better precision, sparing viable segments. In cases where there is still suspicion of borderline ischemic segments, definitive surgical treatment and re-anastomosis of stapled bowel segments can be made during a third- or even a fourth-look operation.

Laparoscopic evaluation of bowel viability after the primary operation has potential pitfalls, as stated in Diagnosis.

Postoperative surveillance in the intensive care unit
During postoperative care, assessment of small bowel viability is not straightforward. Intra-abdominal hypertension (IAH) has been shown to correlate with colonic ischemia (Djavani) after rAAA repair. Although this has not been studied systematically in acute SMA occlusion it has been described that it may lead to abdominal compartment syndrome (ACS) (Sullivan). According to the consensus guidelines of the World Society of the Abdominal Compartment Syndrome (WSACS), it is evidence-based to monitor intra-abdominal pressure in patients treated for acute SMA-occlusion, since in most cases two or more risk-factors for ACS are present (Cheatham et al). Knuesel and co-workers evaluated intra-peritoneal microdialysis in an animal model and reported on significant changes in lactate-pyruvate ratio and mesenteric venous-arterial pCO2 ratio in response to
splanchnic hypoperfusion. These parameters have been demonstrated to correlate to major complications following emergency laparotomy (Verdant). Systemic arterial lactate is often normal due to effective lactate clearance by the liver (Acosta 2007) but may become elevated as a sign of systemic anaerobic metabolism due to septic shock.
Aims of the investigation

The general aim of this thesis is to evaluate diagnostic and therapeutic approaches for acute SMA occlusion. The specific aims are:

- To evaluate previously suggested serum biomarkers for intestinal ischemia in a clinical setting (Paper I).
- To characterize diagnostic laboratory pitfalls in the diagnosis of acute SMA occlusion (paper II).
- To characterize the alteration of gene expression of intestinal tissue cells in response to arterial occlusive ischemia (paper III).
- To study the diagnostic utility and clinical importance of MDCT in patients with acute SMA occlusion (paper IV).
- To study time-trends and management-related factors for outcome after open or endovascular revascularization for acute SMA occlusion (paper V).
Patients and methods

This thesis is based on four clinical papers and one experimental study of intestinal ischemia in animals (paper III). The total number of patients is 353. When cross-matching the patients in paper I, II, IV and V, four patients from paper I were also included in paper V. Furthermore, when correcting for patients included in paper V, 34 additional patients were included in papers II and IV after 2006.

Therefore, the total number of unique patients studied is 262 (67+161+34).

Out of these, 195 suffered from acute arterial occlusion of the SMA.

Table 1. Overview of patients and methods in the four clinical studies

<table>
<thead>
<tr>
<th>Study I</th>
<th>71 patients admitted to Karlskrona Hospital, 2001-2003</th>
<th>Prospective; biomarkers for AMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study II</td>
<td>55 patients with AMI in Malmö University hospital, 2005-2009</td>
<td>Retrospective; laboratory pitfalls in AMI</td>
</tr>
<tr>
<td>Study III</td>
<td>12 research animals (pigs) with experimental AMI</td>
<td>Prospective; mRNA-expression in AMI</td>
</tr>
<tr>
<td>Study IV</td>
<td>67 patients with AMI in Malmö University Hospital, 2004-2008</td>
<td>Retrospective; impact of MDCTiv in patients with AMI</td>
</tr>
<tr>
<td>Study V</td>
<td>161 patients with AMI indentified in SWEDVASC, 1999-2006</td>
<td>Prospective/retrospective; outcome and prong ostic factors in AMI</td>
</tr>
</tbody>
</table>

All studies were given ethical approval through the respective Regional Ethic Committees.

SWEDVASC

The Swedish Vascular Registry (SWEDVASC) started in 1987 and became nationwide by 1994, making it the oldest nationwide vascular registry in the world. The registry includes all 7 university vascular departments, all 20 county hospitals and 5 district hospitals. Vascular procedures are registered regardless whether they are open or endovascular. They are entered in accordance with “intention-to-treat”, i.e. both successful and failed interventions are registered. Patients are usually registered during the hospitalization period for the surgery or endovascular intervention, preferably immediately after the operation or at discharge/death. Variables in
SWEDVASC are registered prospectively, patient and procedural data at operation and clinical outcome after one month and one year. SWEDVASC has been validated by numerous studies with an external validity of 88.4-98.3% and an internal validity of 93-99% for technical variables and 75-95% for medical risk factors (Björck 1996, Kragsterman, Troëng, Ravn). Therefore, the SWEDVASC registry allows assessing procedural and outcome data for vascular surgery in Sweden.

Statistics
In all five papers, non-parametric tests have been used. Mann Whitney-U was used for analyzing differences in continuous variables between groups and Pearson correlation for evaluating correlations between continuous variables. Differences in proportions of nominal variables between groups were analyzed by Fischer’s exact test, Chi-square test or Kendall’s Tau-B test, accordingly. Non-parametric tests have been preferred when sample size was small or when variables were not expected to follow normal distribution.

Uni-variate and multi-variate analysis for survival/mortality have been used when appropriate. Cox-regression and log rank test in Kaplan-Meier analysis have been used to analyze long-term survival.

Paper I focuses on laboratory diagnosis of AMI and statistical analysis of laboratory tests. The performance of a diagnostic test can be described by various statistic terms (Bliss). Sensitivity measures the proportion of actual positives which are correctly identified as such, e.g. the percentage of sick people who are identified as having the condition. Specificity measures the proportion of negatives which are correctly identified, e.g. the percentage of healthy people who are identified as not having the condition. Accuracy measures the total number of true test results (both positive and negative) divided by the total number of observations.

The positive likelihood ratio (LR+) is the frequency of a positive test among the diseased patients (true-positive rate) divided by the frequency of a positive test among non-diseased patients (false-positive rate). This results in the following formula: sensitivity/(1 –specificity). Given this equation, a test with both a sensitivity and specificity of 95% would have a LR+ of 19. The negative likelihood ratio (LR–) is defined as (1 –sensitivity)/specificity. The same test as above would by this equation have a LR- of 0.05. The reason for using likelihood ratios is that it combines both sensitivity and specificity and can be used in small materials, not dependent on the prevalence of the condition (Dujardin).
Results

Study I

71 patients admitted to the surgical department (Blekinge County Hospital, Karlskrona) were studied prospectively during a 2-year period between 2001 and 2003. The inclusion criteria were: patient older than 50 years of age and hospitalized for acute abdominal pain, blood sampling within 24 h of the onset of the pain, and a pain intensity score of 5 or more on a 10-graded visual analogue scale. Blood was sampled at presentation and prior to surgery in all cases. Blood samples were centrifuged and the detached citrated plasma was stored in a freezer at –80°C, and was later analyzed for various biomarkers. Biomarkers significantly associated with intestinal ischemia according to Mann Whitney-U test were analyzed with respect to negative and positive likelihood ratio for AMI. Four different tests for D-dimer were compared and factors influencing mortality were included in a multivariate analysis.

Results

D-dimer was associated with intestinal ischemia (p=0.001) independently of which assay was used. No patient presenting with a normal D-dimer had intestinal ischemia. D-dimer >0.9 mg/L had a specificity, sensitivity and accuracy of 82 %, 60 % and 79 %, respectively. Total LD, isoenzymes of LD 1–4 and liver isoenzyme of ALP (ALP liver) were significantly higher in patients with intestinal ischemia, and accuracies for LD 2 (cut-off 2.3 mkat/L) and ALP liver (cut-off 0.7 mkat/L) were 69 % and 66 %, respectively.

Based on these data, D-dimer may be used as an exclusion test for intestinal ischemia, but lacks specificity. The other plasma biomarkers in this study had insufficient accuracy for this group of patients. In-hospital mortality among patients with (n=10) and without (n=61) intestinal ischemia were 40 % and 3 %, respectively (p=0.003). In the multivariate analysis, only intestinal infarction remained as an independent predictor for mortality.
Comments on the results from paper I

This study expands on earlier findings, stating that a normal D-dimer concentration in the early stages of AMI can be used as an exclusion test. Furthermore, commercially available test kits from several different manufacturers could all be used as an exclusion tests. This is an important finding, addressing the transferability of results since different hospitals use different assay kits. The results concerning LR+ for the other biomarkers were less favourable and suggest that they are unlikely to be clinically useful. At any rate, waiting for such test results in the emergency room setting appears doubtful, an issue further addressed in paper II. A limitation in this study was the small sample size, which could lead to a type II error.

Study II

Methods

The case-records of 55 patients with diagnosis of acute SMA occlusion were retrieved from the local endovascular database and the in-hospital registry during a four-year period between November 1, 2005, and October 31, 2009 at Malmö University Hospital. The diagnosis of acute SMA occlusion (n = 55) was established after CT scan with intravenous contrast enhancement at initial evaluation or at re-evaluation in all but one patient, who was diagnosed at laparotomy. Each CT angiography was scrutinized and re-evaluated by the study collaborators to define the underlying pathology in the mesenteric arterial vasculature. The records were analyzed with regards to clinical presentation, diagnostic procedures including, laboratory markers, radiologic imaging and consultations. Treatment was analyzed regarding surgical technique at primary and secondary procedures. Factors were checked for association with in-hospital mortality with emphasis on possible pitfalls in the diagnostic work-up that could adversely affect outcome.

Results

On admission, Troponin-I (TnI) was above the decision point in 9/19 (47%) patients with embolic occlusion. Elevated pancreatic amylase, normal plasma lactate and renal insufficiency according to creatinine levels were found at admission in 12/45, 13/27 and 28/54 patients, respectively. A TnI above the decision point in 27 patients tested for TnI was associated with a high frequency of referrals from the general surgeon to a specialist in internal medicine (8/10; p= 0.011)) and /or a cardiologist (6/10; p=0.024). The in-hospital mortality rate was 18/55 (33%) patients. Duration of symptoms from onset of disease to proper intervention was not associated with in-hospital mortality (p=0.59) in those 46 assessed patients receiving an
attempt for active intervention. Significant factors leading to a higher survival rate were attempting (p<0.001) and achieving vascular intervention (p<0.001), whereas referrals to the cardiologist (p=0.018) and the presence of myocardial ischemia on ECG (p=0.042) were associated with a higher mortality rate.

There are several potential diagnostic pitfalls in patients with AMI. Troponin-I and pancreas amylase are often elevated and lactate at presentation is normal in approximately 50%.

Comments on the results from study II
This study documents a high frequency of biochemically defined myocardial stress in patients with acute SMA occlusion. In this study, ECG-changes indicating myocardial ischemia and referrals to a cardiologist were both associated with increased short-term mortality whereas time delay to intervention was not. This may reflect the fact that patients with more severe co-morbidity have a lower survival, but also that a referral to an internist in this acute setting does not appear to have any positive effect on outcome.

In a multi-variate analysis of variables associated with in-hospital survival (attempting intestinal revascularization, achieving intestinal revascularization, referral to cardiologist, ECG-changes indicating myocardial ischemia), only attempting and achieving intestinal revascularization remained as independent factors associated with increased survival.

In this study, there was no clear association between time delay and referrals to non-surgical consults. This might be due to a type II error. These patients may have benefited from a quicker path to surgery, being the only independent factor for survival in this material.

Accordingly, the surgeon must not let referrals to medical specialities nor waiting for unnecessary laboratory analysis lead to any delay to surgical treatment, as this is the pivotal factor for outcome.

Study III
Methods
12 landrace male pigs were anaesthetized and scheduled for endovascular intervention with access from the femoral artery. After angiography of the visceral arteries, a catheter was placed in the proximal part of the SMA. Occlusion of the artery (n=6) was then performed by injection of polyvinyl alcohol foam embolization particles. The control group (n=6) underwent the same surgical procedure with the exception that sodium chloride infusion was given instead of the embolization particles. After four hours of ischemia (or sham), laparotomy and intestinal tissue sampling were performed. On the basis of insufficient RNA-quality and/or quantity, three ischemic and three
control pigs were excluded from microarray analysis. Thus, three ischemic and three control pigs were eligible for microarray analysis. Microarray analysis was performed using the GeneChip® whole porcine genome array (Affymetrix Inc, Santa Clara, CA, USA) and validation of gene expression was made by TaqMan® real-time PCR (Applied Biosystems, Foster City, USA).

Results

Seven down-regulated cellular pathways were associated with protein, lipid and carbohydrate metabolism. Seventeen up-regulated pathways were associated with inflammatory and immunological activity, regulation of extracellular matrix and decreasing cellular proliferation. Genes encoding proposed biomarkers for AMI were either up-regulated, such as lactate dehydrogenase and creatine kinase, or down-regulated, such as intestinal fatty acid binding protein and glutathione S-transferase. Genes encoding for tissue-specific intestinal proteins were either down- or up-regulated.

This study describes mRNA-changes of the intestinal tissue cells in response to AMI. Previously suggested biomarkers for AMI showed conflicting expression changes, as did intestinal tissue-specific proteins. Gene expression of these proteins may not be directly linked to their potential use as clinical biomarkers.

Comments on the results from study III

This study demonstrated that microarray gene expression study of intestinal ischemia is feasible. This is in turn may be a valuable method in further evaluating adaptive processes in mesenteric ischemia, such as reperfusion injury and hypoxic preconditioning.

Study IV

Methods

The city of Malmö, Sweden, with 276,000 inhabitants (Swedish Central Bureau of Statistics) in 2006, has one emergency hospital, Malmö University Hospital (MUH). The identification of all in-hospital patients at MUH with the diagnosis of acute SMA occlusion managed operatively or non-operatively during the 4-year study period (1st January 2004 to February 2008) was based on the International Classification of Disease, ICD, 10th edition, code I74.8 and K55 and collected in a computerized registry. The computerized registry at the Department of Pathology, MUH, was used to identify the patients who either had undergone bowel resection with
subsequent histo-pathological evaluation for acute SMA occlusion or deceased patients with acute SMA occlusion. In-hospital deaths were recorded. Sixty-seven patients were included in the study and medical records were analyzed. The impact of MDCT with intravenous contrast (MDCTiv) and CT findings on mortality were analyzed.

Results

In 36 patients that underwent MDCTiv, 24 (67%) were correctly diagnosed with AMI at first evaluation. There was a trend that an inquiry for AMI in the referral letter was associated with higher sensitivity. Patients with suspected or unsuspected AMI were diagnosed by MDCTiv in 18/23 (78%) patients versus 6/13 (46%) patients, respectively (p=0.06). Patients examined by MDCTiv had a lower mortality (42%) as compared to patients examined with plain CT (90% mortality) (p=0.007) or patients not examined by CT (71% mortality) (p=0.031). Patients with and without intestinal pathological findings at MDCTiv had an in-hospital mortality rate of 56% (10/18) and 28% (5/18), respectively (p=0.09). Patients examined by MDCTiv had lower creatinine levels than the plain CT group (p<0.001) and the group not examined by CT (p=0.023).

MDCTiv was the diagnostic method of choice as compared to plain CT.

Comments on results from paper IV

Sensitivity in this study was low, 67% compared to 96% reported by Kirkpatrick et al. This could be due to the fact that only five MDCTiv examinations were biphasic, 18 in arterial phase and 13 in portal phase. Since biphasic examination combines both vascular and tissue criteria it could be more sensitive for mesenteric ischemia than arterial phasing alone. None of the examinations performed under suspicion of AMI (n=23) were biphasic; 18 were in arterial and five in portal phase. In this subgroup, sensitivity was better (78%) but still inferior to previous studies.

The patients not examined by CT had a better survival than the patients examined with plain MDCT. This could be attributed to the fact that a falsely negative MDCT could mislead the clinician to a conservative approach and, in the case of AMI, a fatal outcome. Furthermore, a plain MDCT may have been preferred in acute cases with shock and secondary renal impairment and is therefore more frequently performed in patients with inherently poor prognosis.
Study V

Methods

Through SWEDVASC, 175 operations performed from 1999 to 2006 were identified as having possibly undergone revascularization of the SMA for AMI. Patient charts were collected from 28 hospitals and, after review, 163 revascularizations in 161 patients were identified. Data from patient charts were analyzed, together with prospective registry data.

Results

The number of revascularizations increased fourfold from 10 interventions in 1999 to 41 interventions in 2006. Revascularization with endovascular approach increased during the last three years of the study. D-dimer was tested in 35 patients and was elevated in all cases.

CTA established the diagnosis in 86/153 (56%) of the patients. CTA had a sensitivity for AMI of 80% but if a suspicion of the diagnosis was mentioned in the referral letter, the sensitivity was 92% versus 37% if it was not mentioned (p<0.001). A correct diagnosis by CTA was associated with improved 30-day mortality (p=0.027).

In total, 163 revascularizations were performed, 42 with endovascular and 121 with open approach. Patients treated with open surgery were more likely to have embolic occlusions and atrial fibrillation, whereas the patients treated endovascularly more frequently had symptoms of previous abdominal angina and/or thrombotic occlusions. Patients treated with open surgery had a higher frequency of small and large bowel resection, second-look operation and postoperative short bowel syndrome. All endovascular patients underwent angiographic completion control whereas completion control was performed in only 41/121 procedures (34%) in the open surgery group, mainly with intra-operative Doppler technique. Hence, the quality of completion control was inferior after open surgery compared to endovascular revascularization.

Thirty-day mortality in the open versus the endovascular group was 42% and 28% (p=0.03), respectively. One-year mortality in the open versus endovascular group was 58% and 39% (p=0.02), respectively.

When comparing open and endovascular surgery for long-term survival with log-rank test, endovascular surgery was associated with better survival (p=0.02). However, when entering all variables associated with 1-year survival in multi-variate cox regression analysis, only age and short bowel syndrome remained as independent predictors for death.
Comments – study V

This study has inherited limitations due to the retrospective design, although the patients were entered prospectively into the SWEDVASC. Data suggests that endovascular surgery of AMI is superior in both short- and long term, as compared to open surgery. However, it is difficult to assess whether the increased need for bowel resection in the open group was related to an inferior revascularization, unnecessary bowel resections or if this is due to a more severe intestinal ischemia. Previously suggested risk-factors for decreased survival such as acute thrombotic occlusion and previous vascular surgery (Schoots 2004, Björck 2002) were more frequent in the endovascular group. Time delay from onset of symptoms to treatment was also longer in the endovascular group but this difference was not statistically significant. Furthermore, there were no differences in laboratory markers at presentation, nor any differences in frequencies of pre-existing ischemic heart disease, smoking, hypertension or diabetes.

When comparing open and endovascular surgery for embolic occlusion only, thirty-day and one-year mortality was 37% (32/86) versus 33% (4/12) (p=0.79) and 55% (47/86) versus 50% (6/12) (p=0.762), respectively. Second look surgery, bowel resection and SBS were significantly less frequent in patients treated with endovascular surgery.

When comparing open and endovascular surgery for thrombotic occlusion only, thirty-day and one-year mortality was 56% (15/27) versus 23% (6/26) (p=0.016) and 67% (18/27) versus 35% (9/26) (p=0.020), respectively.

Based on this study, it is not clear whether endovascular surgery for AMI is indeed a superior approach compared to open surgery, and it remains unclear if there was a difference in disease severity between the two groups. In a sub-group analysis of embolic and thrombotic occlusions, endovascular surgery was not significantly better than open surgery concerning mortality outcome in embolic patients, but seemed to imply less surgical trauma. In thrombotic occlusions, open surgery was associated with markedly reduced survival rates, while endovascular surgery was favourable. It seems that the possible advantages of endovascular approach are more apparent in thrombotic occlusions.

Pooled analysis of 195 patients with acute SMA occlusion

Patient characteristics

The 195 patients were identified as described in Methods, page 27. 116/195 (59%) patients were women and the median age was 76 years (IQR 66-82). The frequency of hypertension (HT) was 47% (90/191), ischemic heart
disease (IHD) 41% (80/193), atrial fibrillation (AF) 51% (90/188),
cerebrovascular disease (CVD) 22% (43/195), diabetes mellitus 14%
(27/193) and previous vascular surgery 26% (49/185). Fifty-seven percent
(112/195) of the patients suffered from embolic occlusion and 37% (73/195)
had a thrombotic occlusion. Five patients had an acute SMA dissection, one
had an SMA stent occlusion, and four patients had an indeterminate cause of
SMA occlusion.

Symptoms at presentation
In 195 patients with acute SMA occlusion, median duration of symptoms
from onset to treatment was 30 hours (IQR 13-102). Vomiting and/or
diarrhoea was present in 54% (95/177)) and 52% (89/172), respectively.
Peritonitis was present in 6% (10/166) on admission. The clinical triad could
be denoted in 43% (45/104) of the patients with embolic occlusion whereas
symptoms of previous abdominal angina were denoted in 42% (22/53) of the
patients with thrombotic occlusion.

Laboratory findings
The median plasma lactate was 2.32 mmol/L (IQR 1.73 – 4.95) (ref 0.5 – 2.2
mmol/L) in 48 tested patients. Median C-reactive protein (CRP) was 35
mg/L (IQR 6 – 196; n= 123), white cell blood count (WBC) 14.9 x 10^9/L
(IQR 11.7 – 20.9; n= 134), creatinine 95 µmol/L (IQR 74 – 122; n=128).
It is noteworthy that plasma lactate, CRP and WBC at presentation were
within reference values in 31% (15/48), 23% (28/123), and 10% (14/134),
respectively.
D-dimer was abnormal in all tested patients with AMI (n=45) and remains
as the only laboratory test able to exclude AMI.

Comparing embolic and thrombotic occlusion
When comparing patients with thrombotic or embolic occlusion only, 112
cases of embolic occlusion and 73 cases of thrombotic occlusion were
identified in the pooled analysis. These were analyzed regarding co-
morbidity, symptoms at presentation and laboratory findings. The findings
are outlined in table 2-4. Continuous variables are expressed as median
values with inter quartile range 25-75.
Table 2. Age and co-morbidity in patients with acute embolic or thrombotic SMA occlusion

<table>
<thead>
<tr>
<th></th>
<th>Embolic</th>
<th>Thrombotic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (IQR)</td>
<td>78 (71-85)</td>
<td>70 (63-78)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IHD (%)</td>
<td>52/111 (47)</td>
<td>24/72 (33)</td>
<td>0.09</td>
</tr>
<tr>
<td>AF (%)</td>
<td>84/112 (75)</td>
<td>12/70 (17)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CVD (%)</td>
<td>27/112 (24)</td>
<td>15/73 (21)</td>
<td>0.60</td>
</tr>
<tr>
<td>VASC (%)</td>
<td>18/112 (16)</td>
<td>28/73 (38)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DIAB (%)</td>
<td>19/111 (17)</td>
<td>8/72 (11)</td>
<td>0.29</td>
</tr>
<tr>
<td>HT (%)</td>
<td>80/111 (72)</td>
<td>53/69 (77)</td>
<td>0.60</td>
</tr>
</tbody>
</table>

IHD= ischemic heart disease, AF= atrial fibrillation, CVD= cerebral vascular disease, VASC= previous vascular surgery, DIAB= diabetes, HT= hypertension.

Table 3. Symptoms and findings in patients with acute embolic or thrombotic SMA occlusion

<table>
<thead>
<tr>
<th></th>
<th>Embolic</th>
<th>Thrombotic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration (IQR)</td>
<td>24 (10-72)</td>
<td>62 (22-318)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vomiting (%)</td>
<td>60/108 (56)</td>
<td>34/62 (55)</td>
<td>1.0</td>
</tr>
<tr>
<td>Diarrhoea (%)</td>
<td>53/106 (50)</td>
<td>34/61 (56)</td>
<td>0.52</td>
</tr>
<tr>
<td>Peritonitis (%)</td>
<td>6/102 (6)</td>
<td>3/59 (5)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Duration= time in hours from onset of symptoms to revascularization.

Table 4. Laboratory findings in patients with acute embolic or thrombotic SMA occlusion

<table>
<thead>
<tr>
<th></th>
<th>Embolic</th>
<th>Thrombotic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC (IQR)</td>
<td>14.9 (11.3-20.7)</td>
<td>15.9 (11.8-22.7)</td>
<td>0.361</td>
</tr>
<tr>
<td>CRP (IQR)</td>
<td>19 (5-138)</td>
<td>99 (20-214)</td>
<td>0.006</td>
</tr>
<tr>
<td>Creatinine (IQR)</td>
<td>102 (81-134)</td>
<td>83 (69-106)</td>
<td>0.002</td>
</tr>
<tr>
<td>Lactate</td>
<td>3.2 (1.85-5.33)</td>
<td>2.7 (1.73-4.89)</td>
<td>0.483</td>
</tr>
</tbody>
</table>

Patients with embolic SMA occlusion are older and more frequently suffer from AF, while patients with thrombotic occlusion often have a history of previous vascular surgery. CVD, diabetes and hypertension are similarly frequent in the two groups but there is trend towards a higher frequency of IHD in the embolic group.

Symptoms and findings at presentation are very similar with no apparent differences between the two groups. The duration from onset of symptoms to treatment is significantly longer in patients with thrombotic occlusion.
Discussion

Clinical presentation
Patients with acute SMA occlusion in this thesis were elderly, with more women affected, and the majority had embolic occlusions, as expected. Interestingly, median time from onset of symptoms to definitive treatment was 30 hrs (IQR 13-102), with a wide range between cases. Embolic patients often presented with symptoms and a history of cardiac illness, while thrombotic patients often have a history of previous vascular surgery. In paper V, time delay was not significantly associated with mortality, which is in contrast with other studies (Kassahun, Kougias). This may reflect that surgical vascular competence and technique, including completion angiography are very important factors for reducing bowel loss and for the survival of these patients, even after a considerable time delay. The nature of occlusion can vary with respect of pathogenesis, site of occlusion and to what extent flow is interrupted. Meanwhile, patients could have great variations in vascular anatomy, influencing the development of collaterals, especially in patients with atherosclerotic disease. It is important to point out that the classical clinical triad for embolic disease was absent in a majority of the embolic patients. Clinical diagnosis remains a real challenge, even for the experienced surgeon.

Laboratory diagnosis
Regarding evaluation of biomarkers in peripheral blood samples, this thesis affirms that D-dimer, in the early phase of the disease, is a valuable exclusion test for acute SMA occlusion, regardless of what assay kit is used. There are several potential diagnostic pitfalls in evaluating acute SMA occlusion, especially regarding TnI and pancreatic amylase, as described in paper II.

Out of the patients described in paper II, elevated TnI above the decision point occurred in 47% and 33% of the embolic and thrombotic patients, respectively. Elevated TnI was associated with increased referrals to the cardiologists, possibly leading to diagnostic delay and increased mortality. TnI may be elevated in a variety of cardiac and non-cardiac diseases (Blich),
and this biochemical finding in patients with acute SMA occlusion is probably secondary to myocardial stress.

Slightly elevated amylase is a potential diagnostic pitfall in patients with AMI, and was elevated in 27% of the patients with acute SMA occlusion.

Lactate, a biomarker described in earlier publications on AMI (Lange, Kassahun), was not helpful in the early diagnosis of AMI because of the low sensitivity of the test, as shown in papers II and V. If elevated, lactate can be an ominous sign of prevailing anaerobic metabolism in any critically ill patient and is, consequently, a negative prognostic factor (Kassahun).

CRP and WBC tests in these patients can be normal in the early course of the disease and cannot be used as an exclusion test. If elevated, they are highly unspecific, and cannot be used to confirm the diagnosis.

Elevated serum creatinine concentration in these patients is seldom caused by pre-existing renal insufficiency (Acosta 2010) but may often reflect a state of dehydration due to vomiting, as well as accumulation of fluid intra-abdominally or intra-luminal in the intestine. An elevated creatinine can be associated with shock, general hypoperfusion and death and is associated with increased mortality in this group of patients (Kougias). In the context of MDCTA, an elevated creatinine might deter the clinician from performing an adequate CT examination, thus affecting outcome, as stated in paper IV. Measures to avoid contrast-induced nephropathy should include volume resuscitation before and after the examination (Ellis). In paper V, no patient who underwent MDCTA (n=101) was dependent on renal replacement therapy at discharge. In the acute setting, the decision of whether or not to proceed with MDCTA in the fragile patient must be in close collaboration between the surgeon and the radiologist and individually tailored to the patient. Some patients may be examined with a lower dose of intravenously administered iodinated contrast without compromising the quality of the imaging (Acosta 2010). It should be remembered, though, that CIN is a rare condition and often self-limiting (Katzberg, Oleinik). A high creatinine level is not an absolute contraindication to proceed with a MDCTA in a patient suspected to suffer from an acute SMA occlusion.

The ultimate goal of finding novel, clinically relevant biomarkers for intestinal ischemia remains elusive so far. The potential of a biomarker to serve as an indicator for AMI does not only involve the tissue response to the injury but other variables as well, such as the amount of biomarker leakage into the blood stream, tissue specificity, liver degradation and antigen integrity in plasma over time. All of the above are major determinants of the clinical relevance of a potential biomarker for intestinal ischemia.
Diagnostic imaging

MDCTA has been the dominant diagnostic method during the time period of this investigation, reflecting the development of CT technique and its applications during the last decade. With a suspicion mentioned in the referral letter, MDCTA in paper V had a sensitivity of 92% which is close to what previous studies have reported (Aschoff, Ofer). In paper IV, there was a sensitivity of only 67%, probably reflecting a selection bias whereby all patients in paper V but only 69% (25/36) in paper IV underwent intestinal revascularization. MDCTA provides the surgeon with detailed anatomical information regarding vascular anatomy, possible endovascular or bypass options and pathogenesis. Biphasic MDCTA, the protocol used in studies with high accuracy (Kirkpatrick, Aschoff, Ofer) seems to be the radiologic protocol of choice. It depicts in detail the mesenteric circulation in the arterial phase while it also provides information on the ischemic damage to the bowel tissues in the portal phase. This increases the sensitivity for bowel ischemia and may guide the surgeon in selected cases to withhold from unnecessary laparotomy. In paper V, correct diagnosis by MDCTA was associated with improved 30-day survival (p<0.001), reflecting the clinical importance of fast, accurate and detailed diagnostic imaging.

Open versus endovascular surgery

Open surgery has been and is, by many, still considered the mainstay of treatment for AMI. It is the only way to date to achieve total exposure and inspection of bowel viability in order to determine if bowel resection is necessary. Endovascular revascularization, on the other hand, has many advantages over open revascularization. The surgical trauma can be minimized and thus reduce infection, inflammatory response, postoperative paralysis, opioid medication and immobilization. All of the above could affect the clinical outcome in this group of often elderly patients with multiple co-morbidities.

Schermerhorn et al compared endovascular and bypass surgery for AMI and reported an in-hospital mortality of 16% and 28%, respectively (p<0.01). Apart from this study, there have been little data on comparisons between endovascular and open surgery, especially regarding long-term survival. In paper V, endovascular surgery as compared to open surgery was significantly associated with better survival at 30 days (p=0.03), one year (p=0.02) and at long-term follow-up (log rank p=0.02). In a cox-regression analysis, only age and SBS were independently associated with increased mortality. The patients in the endovascular group had bowel resections less frequently and less extensively, leading to a smaller frequency of SBS.
It is difficult to determine with certainty why the two groups differed regarding to what extent bowel resection was performed. Combining data from the previous study from SWEDVASC regarding SMA occlusion during 1987-1998 (Björck 2002) with paper V is possible although they are two separate studies. Identical study protocols were used and both reports studied the same population in two adjacent time-periods. This can give interesting information on time-trends in acute SMA revascularization. To monitor ongoing time trends in SWEDVASC, registry data for acute SMA revascularization during 2009 was also obtained.

Time trends in acute SMA revascularization show an increase in the total number of revascularizations, with a relative increase of endovascular relative open surgery (Figure 5). According to SWEDVASC data from 2009, endovascular surgery has surpassed open surgery for acute AMI with 29 endovascular versus 24 open revascularizations of the SMA.

![Figure 5. Incidence of open and endovascular revascularizations for acute SMA occlusion in Sweden 1999-2006 and 2009](image)

When comparing surgical treatment between the two periods, there were two endovascular revascularizations in the previous study (Björck 2002) and 42 endovascular procedures in paper V. There was no difference between the previous study and paper V regarding the frequency of primary laparotomy, (97% vs 88%, p=0.11) or bowel resection at primary operation (41% vs 40%, p=0.88). However, second look laparotomy was more frequent in the previous study (68% vs 51%, p=0.02) and bowel resection overall was more frequent (72% vs 51%, p=0.006).

This may indicate that the two groups as a whole had similar severity at the time of primary treatment, since the need for laparotomy and primary
bowel resection were similar. The outcome of the primary procedure, however, seems different. When analyzing the mortality reported in the two studies regarding endovascular or open surgery, the outcome for patients treated with open surgery is not different between the two time-periods (figure 6).

![Figure 6](image)

**Figure 6.** Mortality in acute SMA occlusion in Sweden, comparing the time-periods 1987-1998 with 1999-2006

Judging from this figure, it is evident that the decreased mortality rate reported in paper V, relative to the previous study, is solely a result of better results in the endovascular group. Mortality after open surgery has not changed over time.

In a sub-group analysis of paper V, including patients with either embolic or thrombotic occlusions only, there were no significant differences in mortality between open and endovascular surgery in the embolic group but there was less surgical trauma, less bowel resection and less SBS. In the group with thrombotic occlusions, open surgery was associated with dismal prognosis, both in short- and long-term, while endovascular surgery was favourable. This probably reflects the fact that open surgery for acute SMA thrombotic occlusion is a condition with local pathological changes in the SMA due to atherosclerosis, making open bypass difficult and rendering the SMA prone to dissection. This is more easily avoided with endovascular technique, which also offers the possibility of completion control angiography, evaluating possible additional stenosis and/or thrombosis distally in the SMA.
One factor that has to be considered in this discussion is the impact of local competence and resources at the surgical centres included in this study. Some of them do not have 24-hour access to endovascular intervention and many have not reported more than a few revascularizations during the study period. When analyzing those centres who had reported one or more revascularization per year (≥8), the difference in mortality between endovascular and open surgery persisted (table 5) in university hospitals (centres 1-5). University hospitals have the most resources in terms of intensive care and surgical competence, but there was still a tendency for better outcome in the endovascular group specifically. This suggests that also in a tertiary care setting, endovascular surgery is associated with improved survival. In contrast to this, there was an increased mortality associated with endovascular surgery registered in the secondary centres with only one or two endovascular interventions (6-8). This may reflect the fact that emergency revascularization of the SMA is technically demanding and may not be applicable without sufficient competence and resources. In conclusion, the overall difference in mortality related to endovascular or open surgery reported in paper V, does not seem to be explained by geographical location.

Table 5. Short- and long-term mortality in high-volume centres according to primary revascularization in Sweden 1999-2006

<table>
<thead>
<tr>
<th>Centre</th>
<th>Endo (n)</th>
<th>Mortality 30d/1yr(%)</th>
<th>Open (n)</th>
<th>Mortality 30d/1yr(%)</th>
<th>Total (n)</th>
<th>Mortality 30d/1yr(%)</th>
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</thead>
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<td>-/-</td>
<td>9</td>
<td>33/66</td>
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<td>33/66</td>
</tr>
<tr>
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<td>6</td>
<td>17/33</td>
<td>9</td>
<td>22/33</td>
<td>15</td>
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</tr>
<tr>
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<td>-/-</td>
<td>10</td>
<td>40/70</td>
<td>10</td>
<td>40/70</td>
</tr>
</tbody>
</table>

Completion control and assessment of bowel viability

In paper V, emphasis was put on completion control of the mesenteric revascularization. Different methods have been proposed for evaluating perfusion of the intestines following revascularization, such as palpating mesenteric pulsations, Doppler measurement, fluorescein, transit-time flow measurement and intra-operative duplex. While duplex and fluorescein measurement are more accurate (Oderich 2003, Bulkley), they are
technically demanding and operator-dependent and may therefore be difficult to implement beyond tertiary centres. Doppler has been reported not to add any value to standard clinical judgment (Bulkley). Intra-operative angiography offers the possibility to assess the vascular reconstruction itself, detecting peripheral emboli, iatrogenic dissections, and also flow dynamics to the portal circulation. All of the endovascular procedures in paper V underwent completion control by angiography alone or in combination with bowel inspection during laparotomy. Possibly, angiography offers superior possibilities over the other methods stated above, although this question has not yet been addressed in a prospective clinical study.

Second look laparotomy

In the literature, there are conflicting results concerning the impact of second look on outcome. Bowel resection at second look is reported to be a negative prognostic factor (Kougias). This could be due to selection bias, i.e. the patients with good primary results are not likely to need a bowel resection at second look procedure. On the other hand, cases with the most dismal prognosis may be selected for palliative treatment and are not scheduled for further invasive treatment. In paper V, primary laparotomy was performed in 88% of the total number of revascularizations, with 55% of the endovascular interventions compared to 100% of the open interventions (p<0.001). Second look laparotomy was only performed in 51% of the cases, with 31% and 67% in the endovascular and open surgery group, respectively (p<0.001). Given the favourable outcome in the endovascular group, based on these data, second look cannot be considered mandatory treatment for all patients with AMI. The decision to perform a second look or not should be based on the individual patient at hand considering the potential benefits and risks of another invasive procedure.

When second look laparotomy is considered, any resected bowel at primary operation should be left stapled off and the reconstruction of any bowel anastomosis or stoma should be performed at second look (Freeman). The bowel ends are either better circulated at second-look or there has been a clearer resection border between irreversible bowel gangrene and viable bowel. If a decision to perform second look is made, there is no need to perform fascia closure, since this is time-consuming and the fascia will in any case be opened again. The abdomen at first operation can be temporary closed by a running skin suture only, to avoid repeated trauma to the fascia and to have some abdominal decompression to have a beneficial effect on the visceral circulation (Cheatham). It should be emphasized that the principles of damage control surgery and abbreviated laparotomy (Rotondo) should be applied to patients with AMI.
The viscera at primary or second look operation may be swollen due to excessive fluid resuscitation and/or reperfusion oedema and this can make it difficult to close the abdomen without applying damaging pressure to the intra-abdominal tissues. In this case, it may be better to leave the abdomen open with a temporary abdominal closure device such as the vacuum assisted wound closure system (V.A.C® Abdominal Dressing, KCI, San Antonio, Texas, USA), rather than to try to forcefully close the fascia. To avoid lateralization of the bowel wall, the combination with a mesh has been suggested (Petersson). In this way, intra-abdominal hypertension or abdominal compartment syndrome is avoided and full abdominal decompression is achieved, leading to the best possible physiologic state of this very critically ill patient, facilitating abdominal blood perfusion (Ivatury).

Postoperative care

Very little data on optimal postoperative treatment for AMI is available in the literature. Massive fluid resuscitation to optimize cardiac output is often required due to great loss.

There are reports on recommended use of vasopressors and avoiding pure α-adrenergic stimulators, as this could further exacerbate mesenteric vasospasm and hypoperfusion (Alexander). In patients with shock, a combination of norepinephrine with dobutamine seems appropriate as discussed in Pharmacological treatment (Sun). This regimen combines optimizing mean arterial pressure (norepinephrine) with maximizing cardiac output and oxygen delivery to the intestine (dobutamine).

Pain management is often challenging in these patients and an epidural analgesia may reduce opioid requirements, contributing to respiratory and gastrointestinal function as well as mobilization (Rigg). An effective epidural analgesia also reduces the intra-abdominal pressure (Hakobyan), thus contributing to a better mesenteric perfusion (Spackman).

The issue of maintaining the patient on ventilator treatment as a bridge to a second-look operation, or to extubate between the operations has not been studied. Ventilator treatment with positive end-expiratory pressure has been shown to reduce abdominal perfusion pressure (APP) (Putensen). Ventilator treatment often requires continuous administration of a sedative agent such as midazolam which may further reduce APP by a decrease in systemic arterial pressure (Lamblin). This is often treated with vasopressors which may exacerbate APP even further. According to this reasoning, APP may increase if the patient is extubated while awaiting the second look operation, assuming that the patient is respiratory fit for extubation and pain management is adequate. Another main advantage in performing extubation until the second look procedure is that clinical assessment of the abdomen
becomes possible, with the potential benefit of being able to withhold unnecessary laparotomies in stable, pain-free patients.

**Future perspectives**

With an increasingly geriatric population, the incidence of acute thromboembolic occlusion of the SMA is likely to increase. Computed tomography development will continue and with the increased demand to streamline patient-flow in the emergency departments, it is likely that even more surgical patients will be examined with MDCT at presentation. This may result in an increased detection rate of AMI among patients with acute abdominal pain.

All of the above will challenge the medical community to improve on the persistingly poor prognosis of this condition. Future studies should address some of the questions highlighted in this thesis:

- Is there a biomarker for AMI with better accuracy than those available today?
- Should acute SMA occlusion revascularization primarily be open or endovascular?
- On what grounds should second look procedure be performed?
- How can we improve the postoperative/ICU treatment of these patients?
Conclusions:

- There is to date no biomarker with sufficient accuracy to detect acute mesenteric ischemia.

- Elevated Troponin-I and Amylase are laboratory pitfalls in the diagnosis of AMI and misinterpretation of these test results may have a negative impact on outcome.

- In response to acute mesenteric ischemia, the intestinal tissue cells alter their gene expression, up-regulating genes involved in inflammatory and stress response pathways and down-regulating genes involved in carbohydrate and lipid metabolism.

- How the MDCTA is performed and interpreted have major implications on the clinical outcome in AMI patients suffering from acute SMA occlusion.

- Analysis of patients registered in SWEDVASC shows that the number of patients treated with acute SMA revascularization increases over time, and that endovascular treatment is associated with an improved survival in both short- and long term.
Populärvetenskaplig sammanfattning

Akut blodpropp i övre tarmkäxpulsådern – diagnos och behandling

Tarmens blodförsörjning kommer i huvudsak av tre pulsådor (artärer); I) celiaka-artären, som försörjer tolvfingerarmen, lever, bukspottskörtel och mjälte, II) den övre tarmkäxsartären som försörjer hela tunntarmen och den övre halvan av tjocktarmen, samt III) den nedre tarmkäxsartären, som försörjer den nedre halvan av tjocktarmen samt ändtarmen. Samtliga dessa artärer utgår i normalfallet direkt från den stora kroppspulsådern. Denna avhandling handlar om det akuta stopp för blodflödet som kan uppstå i den övre tarmkäxsartären, eller superior mesenteric artery (SMA), som den heter på engelska.

Liksom i andra artärer i kroppen kan detta blodkärl drabbas av åderförkalkning och blodproppar. Blodproppen kan antingen uppstå lokalt i kärlväggen, oftast till följd av åderförkalkning, och kallas då trombos. En propp kan även uppstå genom att en bit levrat blod, en emboli, transporterades med blodflödet till SMA och kan då fastna där och förhindra blodflödet till tunntarmen. Om inte detta åtgärdas och blodflödet kan återställas där tarmvävnaden i syrebrist, så kallad tarminfarkt. Detta i sin tur leder till att tarmen spricker och ger upphov till en svår blodförgiftning som obehändad leder till döden.

Denna sjukdom är relativt ovanlig och drabbar företrädesvis äldre personer med en tidigare sjukdomshistoria innehållande tecken på hjärt-kärlsjukdom, såsom högt blodtryck, tidigare hjärtinfarkt, förmaksslimmer eller fönstertittarsjuka. Tyvärr saknas mycket kunskap om hur akut blodpropp i SMA ska behandlas på bästa sätt och prognosen är relativt dålig om man jämför med andra svåra sjukdomar såsom hjärtinfarkt, brusten kroppspulsåder eller bröstcancer.

Ett av de stora problemen för sjukvården är att ställa en snabb och tillförlitlig diagnos av stopp i SMA. Plötsligt påkommen buksmärta är det vanligaste symtomet, ofta i kombination med kräkningar och diarré. Det finns inga tillförlitliga blodprov som kan påvisa förekomsten av stopp i SMA. Därför måste den behandlande läkaren i det första skedet helt fokusera på att få en noggrann sjukdomshistoria från sin patient samt att göra en noggrann klinisk undersökning.

Om diagnosen akut stopp i SMA fastställts, måste den omedelbart behandlas. Detta kan ske genom öppen kirurgi eller via röntgenstyrta borttagande av blodproppen via instrument som förs in via artären i handled,

**Delarbete I och II – diagnos genom blodprovstagnation**
I dessa delar studerades hur olika blodprovsanalyser kan användas vid handläggningen av akut SMA stopp. I studie I samlades blodprover in från 71 patienter med misstanke om tarminfarkt. 10 av dessa visade sig sedan ha tarminfarkt och ingen av dessa hade ett normalt värde av D-dimer (en nedbrytningsprodukt som bildas då blodet levrar sig). Detta prov kunde därför användas för att utesluta diagnosen. Vidare testades ett flertal andra blodprov där tidigare studier indikerat att de kunde vara till nytta för att upptäcka det här tillståndet. Ingen av dessa blodprov visade sig vara tillräckligt bra för att kunna tillföra något ytterligare för att i ett tidigt stadium kunna upptäcka den här sjukdomen.

Troponin-I, ett välkänt prov för hjärtinfarkt, och amylas, vilket bland annat används för att upptäcka inflammation i bukspottskörteln, var ofta förhöjt hos patienter med stopp i SMA, trots att vidare utredning inte påvisade någon hjärtinfarkt eller bukspottskörtelinflammation. Dessa två blodprover kan alltså vara falskt förhöjda hos dessa patienter och kan potentiellt fördröja diagnos och behandling, vilket i sin tur kan vara mycket negativt för patientens prognos.

**Delarbete III – hur tarmvävnaden reagerar på tarminfarkt**
I denna studie undersökte hur celler i tarmväggen ändrade sin produktion av proteiner och andra cellulära funktioner när tarmväggen utsattes för ett stopp i SMA. I en försöksmodell med grisar sövda i narkos fick hälften av grisarna ett konstgjort stopp i SMA via en kateter i en av ljumskartärerna. Sedan analyserades tarmväggens celler utifrån hur de hade aktiverat olika gener som svar på tarminfarkten. Det visade sig att cellerna minskade aktiviteten hos de gener som var kopplade till ökad ämnesomsättning, men ökade aktiviteten hos de gener som var kopplade till inflammation och minskad ämnesomsättning för att på sätt kunna minska sitt behov av syre och näring och kunna överleva under den pågående tarminfarkten. I analysen upptäcktes inget uppenbart protein som skulle kunna användas vidare i studier för att utveckla ett blodprov för att kunna upptäcka tarminfarkt.

**Delarbete IV – på vilket sätt kan skiktröntgen påverka handläggningen av dessa patienter?**
67 patienter på Malmö Universitetssjukhus med akut SMA stopp ingick i studien. Av dessa hade 36 patienter undersöks med skiktröntgen med kontrast, vilket kunde ge detaljerade bilder över artärcirkulationen i buken.
När dessa 36 patienter jämfördes med den övriga gruppen visade det sig att gruppen som undersöks med skiktröntgen med kontrast överlevde i högre grad än depatienter som undersöktes utan kontrast eller inte fick någon skiktröntgen alls. Skiktröntgen med kontrast kunde upptäcka SMA stopp i två fall av tre men detta ökade till fyra fall av fem om en misstanke om tarminfarkt nämndes i remissen till röntgenläkaren. Studien visade att skiktröntgen med kontrast var förknippat med bättre överlevnad hos dessa patienter och bör därför vara förstahands valet vid diagnos av akut SMA stopp.

**Delarbete V – trender i öppen och endovaskulär behandling i Sverige**


**Sammansatt analys av 195 patienter med akut stopp av SMA från studie I-II och IV-V**

Hjärt- och kärlsjukdom var vanligt förekommande hos dessa patienter, cirka hälften hade högt blodtryck eller förmaksflimmer, 2/5 hade tidigare kärlkramp eller hjärtinfarkt. En fjärdel av patienterna hade tidigare genomgått någon form av kärlkirurgi och 1/5 hade haft slaganfall.

Hjärtsjukdom var vanligare hos patienter med emboli medan tidigare kärlkirurgi var vanligare i gruppen med trombos. Cirka hälften av patienterna hade kräkts och/eller haft diarré. Patienter med trombos hade som regel haft ont en längre tid innan operation, jämfört med de som haft en emboli.
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