

Does calcium score in great pelvic vessels predict colorectal anastomotic leakage? A prospective study of one hundred anastomoses

Mohammad Tayefeh Norooz¹, Hamid Moradi², Mahdi Safdarian³, Fariba Jahangiri⁴, Hadi Ahmadi Amoli⁵

(1) Surgery Department, Sina Hospital, Sina Trauma and Surgery Research Center, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran ; (2) Sina Trauma and Surgery Research Center, Sina Hospital, Sina Trauma and Surgery Research Center, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran ; (3) Sina Trauma and Surgery Research Center, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran ; (4) Surgery Department, Iran University of Medical Sciences, Tehran, Iran ; (5) Surgery Department, Sina Hospital, Sina Trauma and Surgery Research Center, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran.

Abstract

Background and study aims : Anastomotic leakage is one of the most severe surgical complications following surgery. This prospective study was designed to investigate an association between the calcification in the descending aorta and its major branches using a calcium-scoring software and colorectal anastomotic leakage.

Patients and methods : From January 2012 to March 2013, one hundred patients underwent surgeries involving colorectal anastomosis procedures. Calcium score in descending aorta and great pelvic vessels was measured using the Syngo-CT 2006G-W software. A questionnaire was completed containing demographic and underlying risk factors suspicious to be associated with anastomotic leakage, in addition to surgical characteristics data.

Results : 55 males and 45 females entered the study with the mean age of 63.70 ± 7.17 years. The average duration time of surgery was 149.30 ± 20.24 minutes. The type of surgery was elective for 90 patients and emergency for 10 others. The mean calcium score was higher in greater arteries as in abdominal aorta and common iliac arteries in comparison to the other pelvic vessels. Comparing two groups of patients with and without anastomotic leakage, the calcium score was higher in descending aorta and all great pelvic vessels of patients with colorectal anastomotic leakage ($P < 0.001$). One patient (1%) died due to postoperative anastomotic leakage two weeks after the surgery.

Conclusions : Atherosclerotic calcification in the descending aorta and its major branches can be considered as a risk factor in the development of colorectal anastomotic leakage. (*Acta gastroenterol. belg.*, 2016, 79, 415-420).

Key words : anastomotic leakage, calcium score, colorectal.

Introduction

Colorectal anastomotic leakage remains a serious complication after surgery leading to high morbidity rates. Several risk factors have been suggested to be involved in postsurgical anastomotic leakage in surgery such as bacteria (1), prolonged operative time (2-5), high ASA (American Society of Anesthesiologists) score (3,6-8), high body mass index (BMI) (4,9), emergency operation

(7), total colectomy (3), prophylactic drainage (4,10), smoking (9,11) and alcohol abuse (11), cardiovascular disease (5), preoperative steroid use (12), preoperative chemoradiotherapy (2,5), type of anastomotic suture (13).

Although various risk factors of colorectal anastomotic leakage have been extensively studied, no significant reduction has been observed over the last years. The incidence rate of this complication is still high and varies from 2.5% to 20% in the literature (14-19) which means the practical risk factors of colorectal anastomotic leakage have not been well-established yet. Therefore, a better understanding of risk factors for developing anastomotic leakage in surgery is still an important issue for research.

Local ischemia is one of the anastomotic leakage causes after surgery (20,21). Insufficient arterial blood supply caused by atherosclerosis has been suggested to have a negative effect on anastomotic healing (19).

Nowadays, it has become popular to quantify calcification due to atherosclerosis in computed tomography (CT) scan using calcium-scoring software. Recently, there has been interest in the measurement of calcium score in carotid (22-25) and coronary (26-31) arteries to predict the extent and severity of atherosclerosis to predict the prognosis of the patients.

Correspondence to : Hadi Ahmadi Amoli, M.D., Associate Professor, Surgery Department, Sina Hospital, Sina Trauma and Surgery Research Center, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran.
E-mail : mahdysafdaryan@yahoo.com

Submission date : 19/10/2015
Acceptance date : 17/05/2016

A retrospective study by Komen et al. has evaluated calcium score in great pelvic arteries as a risk factor for atherosclerosis which can result in colorectal anastomotic leakage (18). This score represents the severity of atherosclerosis in the detecting arteries, as a main predicting factor for ischemia.

Here we designed a prospective cross-sectional study to evaluate calcium score in the descending aorta and its major branches as a probable risk factor for predicting colorectal anastomotic leakage at a preclinical stage. Our null hypothesis is that there would be an association between calcium score in pelvic arteries and colorectal anastomotic leakage risk.

Methods and materials

This prospective cross-sectional study was approved by the local ethics committee of Sina Trauma and Surgery Research Center, Sina Hospital, Tehran University of Medical Sciences (TUMS). All patients with rectal or colon cancers undergoing colon resection with colocolic or ileocolic anastomoses regardless of receiving radiotherapy prior to the surgery from February 2012 to May 2014 in Sina University Hospital were recruited in this study. Patients with ileal pouch-anal anastomosis were excluded from the study. All included patients signed an informal consent.

Contrast-enhanced abdominal CT scan with a 5-mm slice thickness was collected from all patients before surgery except in emergency situations in which CT scan was performed postoperatively. Calcium score was subsequently processed to generate using a standard calcium-scoring software (*Syngo-CT 2006G-W software*; Siemens, Forchheim, Germany) by an expert radiologist based on the preoperative CT scan, in the following arteries; descending aorta lower than the level of L1-L2, right and left common iliac arteries, right and left internal and external iliac arteries and the superior mesenteric artery. The lower threshold for determining calcium score was considered 500 Hounsfield units. Another abdominal and pelvic CT scan with oral and intravenous contrast was performed only in patients with clinical suspicion of anastomotic leakage to confirm the anastomotic leakage based on their signs and symptoms. Any patient with the diagnosis of abscess in imaging, purulent discharge from the anastomosis site, gastrointestinal discharge from drains or extravasation of contrast in CT scan was considered as a case of anastomosis leakage. In addition, patients requiring surgical or radiological drainage and those who had small abscesses in CT scan and were decided for antibiotic therapy only without drainage were also considered as anastomotic leakage.

Protective loop ileostomy was done for all patients who had received neoadjuvant chemoradiotherapy prior to the surgery. A questionnaire containing patient and operation related variables including age, BMI, sex, comorbid diseases like hypertension (systolic blood

pressure more than 140 mm Hg or diastolic blood pressure more than 90 mm Hg) and diabetes mellitus, neoadjuvant therapy, use of steroids, smoking, American Society of Anesthesiology (ASA) score, duration of surgery, type of surgery (emergency or elective), type of suture (stapler or hand-sewn), type of anastomotic (end to side or end to end) and anatomical location of the anastomosis was completed.

Mann-Whitney U or chi-square tests in univariate analysis were used to compare between two groups of patients with and without anastomotic leakage. Analysis was performed using *SPSS software version 20*; SPSS Inc, Chicago, Illinois, USA. P values less than 0.05 were considered as statistically significant in all analysis.

Results

One hundred patients (55 males and 45 females) with the mean age of 63.7 ± 7.1 years (ranging from 49 to 76) underwent surgeries involving colorectal anastomosis over a 20-month period. As the main outcome, anastomotic leakage was found in 20 cases (20%) diagnosed clinically and confirmed by abdominopelvic CT scan.

ASA score was I for 35 and II for 65 patients. Other patient-related data are shown in table 1. Comparing the two groups of patients with and without anastomotic leakage, the incidence of anastomotic leakage was significantly higher in males, diabetic patients, smokers and in those who received neoadjuvant chemoradiotherapy prior to the surgery (p values <0.05) (Table 1).

The mean duration time of surgery was 149.3 ± 20.2 minutes (range from 120 to 200). The type of surgery was elective for 90 patients and emergency for 10 others. Table 2 shows the comparison of other surgical characteristics between the two groups of patients with and without anastomotic leakage. The mean duration time of surgery was higher in patients with anastomotic leakage in comparison to those without leakage (p value <0.05). The incidence of anastomotic leakage was significantly higher in patients with emergency surgeries, end-to-end anastomosis and also in rectal anastomoses (p values <0.05) (Table 2).

The mean calcium score was higher in greater arteries as in abdominal aorta and common iliac arteries in comparison to the other pelvic vessels. Figure 1 shows the mean difference of calcium scores in abdominal aorta and great pelvic arteries for the two groups of patients with and without colorectal anastomotic leakage. One patient (1%) died due to anastomotic leakage two weeks after surgery.

Discussion

Different etiological factors including insufficient arterial blood supply, tension on the anastomosis, hematoma or infection at the anastomotic site, and co-morbid factors of the patient as diabetes and atherosclerosis are known to be related to developing

Table 1 — Comparison of patient-related data in two groups of patients with and without colorectal anastomosis leakage

Patient-related data			Anastomosis leakage		P value	
			Positive	Negative		
			20 (20%)	80 (80%)		
Demographic data	Age (Mean±SD) (yr)		63.70 ± 7.17	62.7 ± 9.6	63.9 ± 6.4	0.510
	BMI (Mean±SD) (Kg/m ²)		20.44 ± 1.50	19.7 ± 0.9	20.6 ± 1.5	0.118
	Sex	Male	55 (55%)	15 (27.3%)	40 (72.7%)	0.044
Female		45 (45%)	5 (11.1%)	40 (88.9%)		
Underlying data	Hypertension	Positive	60 (60%)	15 (25%)	45 (75%)	0.126
		Negative	40 (40%)	5 (12.5%)	35 (87.5%)	
	Diabetes mellitus	Positive	20 (20%)	0 (0%)	20 (100%)	0.012
		Negative	80 (80%)	0 (0%)	80 (100%)	
	Steroid use	Positive	15 (15%)	5 (33.3%)	10 (66.7%)	0.161
		Negative	85 (85%)	15 (17.6%)	70 (82.4%)	
	Neoadjuvant chemoradiotherapy	Positive	25 (25%)	11 (44%)	14 (56%)	0.040
		Negative	75 (75%)	9 (12%)	66 (88%)	
Smoking	Positive	40 (40%)	15 (37.5%)	25 (62.5%)	<0.001	
	Negative	60 (60%)	5 (8.3%)	55 (91.7%)		

Table 2 — Comparison of operation-related data between two groups of patients with and without colorectal anastomosis leakage

operation-related data			Anastomosis leakage		P value
			Positive	Negative	
			20 (20%)	80 (80%)	
Duration of surgery (Mean±SD)(min)		149.30±20.24	157.2±17.3	147.3±20.5	0.049
Type of suture	Hand-sewn	40 (40%)	10 (25%)	30 (75%)	0.307
	Stapler	60 (60%)	10 (16.7%)	50 (83.3%)	
Type of surgery	Emergency	10 (10%)	5 (50%)	5 (50%)	0.012
	Elective	90 (90%)	15 (16.7%)	75 (83.3%)	
Type of anastomosis	End to side	40 (40%)	0 (0%)	40 (100%)	0.036
	End to end	60 (60%)	20 (33.3%)	40 (66.6%)	
Anatomical location of the anastomosis	Ascending (right) colon	15 (15%)	0 (0%)	15 (100%)	<0.001
	Descending (left) colon	50 (50%)	5 (10%)	45 (90%)	
	Rectum	20 (20%)	10 (50%)	10 (66.6%)	
	Total colon	15 (15%)	5 (33.3%)	10 (66.7%)	

anastomotic leakage. However, no consensus on the preoperative risk factors exists. CT scan detection of calcium has become a popular technique for assessing atherosclerosis (34). Calcification score actually measures the atherosclerotic load in the vascular route (33,34). Komen et al. retrospectively analyzed calcium score, as a risk factor for colorectal anastomotic leakage, in 122 patients using a CT scan and calcium scoring software. Their results showed that patients with higher calcium scores in the iliac arteries have an increased leakage risk. In their study, calcium score was significantly higher in the left common iliac artery, right common iliac artery, both common iliac arteries together, and the left internal iliac artery. This variable was not significantly different

between the two groups of patients with and without AI in Aorta, left external iliac artery, right internal iliac artery, right external iliac artery, left and right internal iliac arteries (18). As it is shown in figure 1, all the calcium scores were significantly different between the two groups in all assessed arteries including abdominal aorta, both common iliac arteries, both external iliac arteries, both internal iliac arteries, superior mesenteric artery and eventually in all trajectory in our study.

Komen et al reported all the three parameters of calcium score, volume and mass as independent risk factors for colorectal anastomotic leakage. However, the data for calcium volume and mass was not available in our study.

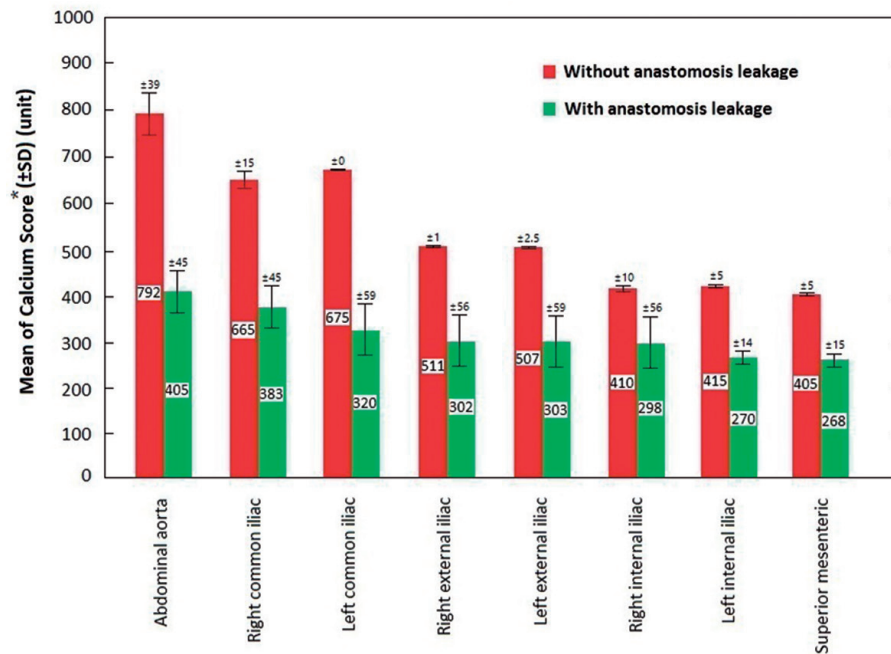


Fig. 1. — Mean of calcium score (\pm SD) in descending aorta and great pelvic vessels of patients with and without colorectal anastomosis leakage

*All the differences were statistically significant (P values <0.001)

On the other hand, male gender, diabetes mellitus, smoking and neoadjuvant chemoradiotherapy from patient-related factors and duration of surgery, type of surgery (emergency vs. elective), type of anastomosis (end to side vs. end to end) and anatomical location of the anastomosis from the operation-related data were significantly different between the two groups in our study. However, none of the scored patient- and operation-related factors were significantly different between the two groups of patients with and without anastomotic leakage in Komen's. Moreover, the superior mesenteric artery, which has the main part of colorectal region blood supply was not evaluated by Komen et al.

Although this study was designed to measure calcification in great pelvic vessels, some important points should be taking into consideration. First, atherosclerosis of micro vessels is very important in local perfusion and calcification in major vessels might be reflecting vascular diseases in the microvasculature. Second, hypoperfusion might already be present without calcification, since atherosclerosis is not always calcified but do affect perfusion. In addition, atherosclerosis may just reflect the general condition of the patient increasing the risk of leaking anastomoses, without causing a lower blood supply.

The blood supply of the colorectal region is mainly provided by the superior and inferior mesenteric arteries. Calcium scoring was not possible in inferior mesenteric artery due to its small diameter, but we calculated the calcium score in the superior mesenteric, which was not calculated in Komen's study.

We accept that a colorectal anastomotic leakage rate of 20% is far too high which can be mainly due to less experience of the surgeon especially in rectal region. Comparing our anastomotic leakage rate with those of other studies, Komen et al. reported a rate of 9% among their 122 patients while Kingham et al. reported rate of anastomotic leakage ranging from 2.4% to 19% in different studies although experienced colorectal surgeons often quote 3% to 6% as an acceptable overall leakage rate (35). Kingham also emphasizes that emergency operations are at greater risk for anastomosis breakdown than those procedures performed electively, as in our patients, from ten emergency surgeries, five (50%) had anastomotic leakage.

Considering the main object of the study that would be a comparison of calcification in great vessels between two groups of patients with and without anastomotic leakage, the main limitation of this study would be a high variety of indications and types of anastomoses, so a uniform conclusion may not be drawn.

As a summary, our findings recommend that calcification in the descending aorta and its major branches can be considered as a risk factor in the development of colorectal anastomotic leakage. Preoperative calcium score calculation in great arteries, along with the other underlying factors, can be helpful in predicting the outcome of anastomosis. Prospective studies with a larger number of patients should be performed and additional parameters should be studied to explore the full diagnostic potential of this method in preventing colorectal anastomotic dehiscence.

Conflict of interest

The authors declare that they have no conflict of interest.

Acknowledgment

This study is the surgery specialty thesis of Dr Hamid Moradi under supervision of Dr Hadi Ahmadi Amoli. The authors wish to thank Mrs. Bitia Pourmand (Sina Hospital, Urology Research Center) for her assistance in preparing the manuscript. We should also thank Dr Soheil Saadat for his kind assistance in analysing the data. The authors wish to thank the reviewers of Acta Gastro-enterologica Belgica for their support and feedback.

References

- LEE D.S., RYU J.A., CHUNG C.R., YANG J., JEON K., SUH G.Y., *et al.* Risk factors for acquisition of multidrug-resistant bacteria in patients with anastomotic leakage after colorectal cancer surgery. *International journal of colorectal disease*, 2015, **30(4)** : 497-504. Epub 2015/03/05.
- MATTHIESSEN P., HALLBOOK O., ANDERSSON M., RUTEGARD J., SJODAHL R. Risk factors for anastomotic leakage after anterior resection of the rectum. *Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland*, 2004, **6(6)** : 462-9. Epub 2004/11/04.
- BUCHS N.C., GERVAZ P., SECIC M., BUCHER P., MUGNIER-KONRAD B., MOREL P. Incidence, consequences, and risk factors for anastomotic dehiscence after colorectal surgery : a prospective monocentric study. *International journal of colorectal disease*, 2008, **23(3)** : 265-70. Epub 2007/11/24.
- KOMEN N., DIJK J.W., LALMAHOMED Z., KLOP K., HOP W., KLEINRENSINK G.J., *et al.* After-hours colorectal surgery : a risk factor for anastomotic leakage. *International journal of colorectal disease*, 2009, **24(7)** : 789-95. Epub 2009/03/21.
- MAKELA J.T., KIVINIEMI H., LAITINEN S. Risk factors for anastomotic leakage after left-sided colorectal resection with rectal anastomosis. *Diseases of the colon and rectum*, 2003, **46(5)** : 653-60. Epub 2003/06/07.
- ALVES A., PANIS Y., TRANCART D., REGIMBEAU J.M., POCARD M., VALLEUR P. Factors associated with clinically significant anastomotic leakage after large bowel resection : multivariate analysis of 707 patients. *World journal of surgery*, 2002, **26(4)** : 499-502. Epub 2002/03/23.
- CHOI H.K., LAW W.L., HO J.W. Leakage after resection and intraperitoneal anastomosis for colorectal malignancy : analysis of risk factors. *Diseases of the colon and rectum*, 2006, **49(11)** : 1719-25. Epub 2006/10/20.
- Erdas E., Zedda A., Pitzalis A., Scano D., Barbarossa M., Aresu S., *et al.* [Anastomotic leak following colorectal surgery : incidence, risk factors and treatment]. *Chirurgia italiana*, 2009, **61(4)** : 407-17. Epub 2009/10/23. La deiscenza anastomotica in chirurgia coloretale : incidenza, fattori di rischio e trattamento.
- NICKELSEN T.N., JORGENSEN T., KRONBORG O. Lifestyle and 30-day complications to surgery for colorectal cancer. *Acta oncologica (Stockholm, Sweden)*, 2005, **44(3)** : 218-23. Epub 2005/08/04.
- JESUS E.C., KARLICZEK A., MATOS D., CASTRO A.A., ATALLAH A.N. Prophylactic anastomotic drainage for colorectal surgery. *The Cochrane database of systematic reviews*, 2004, **(4)** : CD002100. Epub 2004/10/21.
- SORENSEN L.T., JORGENSEN T., KIRKEBY L.T., SKOVDAL J., VENNITS B., WILLE-JORGENSEN P. Smoking and alcohol abuse are major risk factors for anastomotic leakage in colorectal surgery. *The British journal of surgery*, 1999, **86(7)** : 927-31. Epub 1999/07/27.
- KONISHI T., WATANABE T., KISHIMOTO J., NAGAWA H. Risk factors for anastomotic leakage after surgery for colorectal cancer : results of prospective surveillance. *Journal of the American College of Surgeons*, 2006, **202(3)** : 439-44. Epub 2006/02/28.
- Lustosa S.A., Matos D., Atallah AN, Castro AA. Stapled versus handsewn methods for colorectal anastomosis surgery. The Cochrane database of systematic reviews. 2001(3) : CD003144. Epub 2001/11/01.
- HAGMULLER E, LORENZ D, WERTHMANN K., TREDE M. [Uses and risks of drainage following elective colon resection. A prospective, randomized and controlled clinical study]. *Der Chirurg. Zeitschrift fur alle Gebiete der operativen Medizin*, 1990, **61(4)** : 266-71. Epub 1990/04/01. Nutzen und Risiken einer Drainage nach elektiven Colonresektionen. Eine prospektive, randomisierte und kontrollierte klinische Studie.
- HYMAN N., MANCHESTER T.L., OSLER T., BURNS B., CATALDO P.A. Anastomotic leaks after intestinal anastomosis : it's later than you think. *Annals of surgery*, 2007, **245(2)** : 254-8. Epub 2007/01/25.
- MATTHIESSEN P., HALLBOOK O., RUTEGARD J., SIMERT G., SJODAHL R. Defunctioning stoma reduces symptomatic anastomotic leakage after low anterior resection of the rectum for cancer : a randomized multicenter trial. *Annals of surgery*, 2007, **246(2)** : 207-14. Epub 2007/08/02.
- SAGAR P.M., COUSE N., KERIN M., MAY J., MACFIE J. Randomized trial of drainage of colorectal anastomosis. *The British journal of surgery*, 1993, **80(6)** : 769-71. Epub 1993/06/01.
- KOMEN N., KLITSIE P., DIJK J.W., SLIEKER J., HERMANS J., HAVENGA K., *et al.* Calcium score : a new risk factor for colorectal anastomotic leakage. *American journal of surgery*, 2011, **201(6)** : 759-65. Epub 2010/09/28.
- FOSTER M.E., BRENNAN S.S., MORGAN A., LEAPER D.J. Colonic ischaemia and anastomotic healing. *European surgical research Europaische chirurgische Forschung Recherches chirurgicales europeennes*, 1985, **17(3)** : 133-9. Epub 1985/01/01.
- SCHARFF J.R., LONGO W.E., VARTANIAN S.M., JACOBS D.L., BAHADURSINGH A.N., KAMINSKI D.L. Ischemic colitis : spectrum of disease and outcome. *Surgery*, 2003, **134(4)** : 624-9 ; discussion 9-30. Epub 2003/11/08.
- GREENWALD D.A., BRANDT L.J., REINUS J.F. Ischemic bowel disease in the elderly. *Gastroenterology clinics of North America*, 2001, **30(2)** : 445-73. Epub 2001/07/04.
- HO J.S., CANNADAY J.J., BARLOW C.E., REINHARDT D.B., WADE W.A. Computed tomography detection of carotid calcium and subclinical carotid atherosclerosis. *The international journal of cardiovascular imaging*, 2012, **28(6)** : 1601-7. Epub 2011/11/22.
- SARIKAYA B., LOHMAN B., MCKINNEY A.M., GADANI S., IRFAN M., LUCATO L. Correlation between carotid bifurcation calcium burden on non-enhanced CT and percentage stenosis, as confirmed by digital subtraction angiography. *The British journal of radiology*, 2012, **85(1015)** : e284-92. Epub 2011/09/08.
- AL-MUTAIRY A., SOLIMAN A., MELHEM E.R., HURST R., KREJZA J., AL-OKAILI R. Carotid calcium scoring may correlate in males with the traditional Framingham epidemiologic risk variables for stroke. *Surgical neurology*, 2009, **71(2)** : 197-200 ; discussion 1. Epub 2008/02/23.
- LESTER S.J., ELEID M.F., KHANDHERIA B.K., HURST R.T. Carotid intima-media thickness and coronary artery calcium score as indications of subclinical atherosclerosis. *Mayo Clinic proceedings*, 2009, **84(3)** : 229-33. Epub 2009/03/03.
- LAI H.M., HOLTZMAN D., ARONOW W.S., DELUCA A.J., AHN C., MATAYEV S., *et al.* Association of coronary artery calcium with severity of myocardial ischemia in left anterior descending, left circumflex, and right coronary artery territories. *Clinical cardiology*, 2012, **35(1)** : 61-3. Epub 2011/11/16.
- VERSTEYLEN M.O., JOOSEN I.A., WINKENS M.H., LAUFER E.M., SNIJDER R.J., WILDBERGER J.E., *et al.* Combined use of exercise electrocardiography, coronary calcium score and cardiac CT angiography for the prediction of major cardiovascular events in patients presenting with stable chest pain. *International journal of cardiology*, 2013, **167(1)** : 121-5. Epub 2012/01/10.
- ARBAB-ZADEH A., MILLER J.M., ROCHITTE C.E., DEWEY M., NIINUMA H., GOTTLIEB I., *et al.* Diagnostic accuracy of computed tomography coronary angiography according to pre-test probability of coronary artery disease and severity of coronary arterial calcification. The CORE-64 (Coronary Artery Evaluation Using 64-Row Multidetector Computed Tomography Angiography) International Multicenter Study. *Journal of the American College of Cardiology*, 2012, **59(4)** : 379-87. Epub 2012/01/21.
- THANASSOULIS G., PELOSO G.M., PENCINA M.J., HOFFMANN U., FOX C.S., CUPPLES L.A., *et al.* A genetic risk score is associated with incident cardiovascular disease and coronary artery calcium : the Framingham Heart Study. *Circulation Cardiovascular genetics*, 2012, **5(1)** : 113-21. Epub 2012/01/12.
- YAMAMOTO H., OHASHI N., ISHIBASHI K., UTSUNOMIYA H., KUNITA E., OKA T., *et al.* Coronary calcium score as a predictor for coronary artery disease and cardiac events in Japanese high-risk patients. *Circulation journal : official journal of the Japanese Circulation Society*, 2011, **75(10)** : 2424-31. Epub 2011/07/23.
- UEDA H., HARIMOTO K., TOMOYAMA S., TAMARU H., MIYAWAKI M., MITSUSADA N., *et al.* Relation of cardiovascular risk factors and angina status to obstructive coronary artery disease according to categorical

- coronary artery calcium score. *Heart and vessels*, 2012, **27(2)** : 128-34. Epub 2011/03/19.
32. GLODNY B., NASSERI P., PLAIKNER M., UNTERHOLZNER V., REHDER P., KOPPELSTATTER C., *et al.* Prediction of the presence of renal artery stenosis by calcium scoring of the abdominal aorta. *European journal of radiology*, 2012, **81(7)** : 1393-9. Epub 2011/03/29.
33. GREENLAND P., BONOW R.O., BRUNDAGE B.H., BUDOFF M.J., EISENBERG M.J., GRUNDY S.M., *et al.* ACCF/AHA 2007 clinical expert consensus document on coronary artery calcium scoring by computed tomography in global cardiovascular risk assessment and in evaluation of patients with chest pain : a report of the American College of Cardiology Foundation Clinical Expert Consensus Task Force (ACCF/AHA Writing Committee to Update the 2000 Expert Consensus Document on Electron Beam Computed Tomography) developed in collaboration with the Society of Atherosclerosis Imaging and Prevention and the Society of Cardiovascular Computed Tomography. *Journal of the American College of Cardiology*, 2007, **49(3)** : 378-402. Epub 2007/01/24.
34. RUMBERGER J.A., SIMONS D.B., FITZPATRICK L.A., SHEEDY P.F., SCHWARTZ R.S. Coronary artery calcium area by electron-beam computed tomography and coronary atherosclerotic plaque area. A histopathologic correlative study. *Circulation*, 1995, **92(8)** : 2157-62. Epub 1995/10/15.
35. KINGHAM T.P., PACHTER H.L. Colonic anastomotic leak : risk factors, diagnosis, and treatment. *Journal of the American College of Surgeons*, 2009, **208(2)** : 269-78. Epub 2009/02/21.