

ANSWERING REVIEWERS

December 14, 2012

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 1223-edited.doc).

Title: Does arterial encasement on CT always mean invasion at surgery in pancreatic cancer? If not, how can we assess resectability and what is the strategy?

Authors Vyacheslav I. Egorov, Roman V Petrov, Elena N. Solodinina, Gregory G. Karmazanovsky, Natalia S. Starostina, Natalia A. Kuruschkina

Name of Journal: *World Journal of Gastrointestinal Surgery*

ESPS Manuscript NO: 1223

The manuscript has been improved according to the suggestions of reviewers:
1 Format has been updated

2 Revision has been made according to the suggestions of the reviewers 1 and 2
Reviewer 1

Dear Sir, thank you very much for reviewing our manuscript

1. We discussed your comments with my co-authors and we also feel that Discussion is longer than desirable. At the same time we would like to report the substantiated evidence that was not systematically reported before. Considering that we ought to be accurate and comprehensive. We would like the reader to be certain that the authors master all the fine points and intricacies of the problem under review with a view to surgeon, radiologist and gastroenterologist, who contributed all to the text. For this reason, in the discussion we could not pass over the following issues:

- The modern consensus on the problem of arterial involvement in pancreatic cancer
- The accuracy of CT, MRI, endoUS, intraperitoneal and intravenous US for diagnosing that
- The evaluation of the results we have obtained;
- The false-positivity problem in existing reports on evaluation of arterial involvement
- The importance of critical attitude to the intraoperative assessment of resectability in large pancreatic cancer
- The limitations of resectability assessment in every particular department;

- The clinical value of knowing the weak points of CT (as the “gold standard”) in some cases and the typical CT signs of arterial invasion.

The discussion was shorter prior to our communication with 29 of 50 well-known surgeons and radiologists whom we have written on the above mentioned subject. Answering the questions our colleagues raised we have amplified the Discussion to make some points clear (As for example the question of false –negative CT results - R2-resections after crossing of no-return point). That is why we judge it to be critically important to keep the nuances of the discussion as they are.

2. We have shortened the Reference. Nevertheless, neither radiologists, no gastroenterologists, no surgeons consider reasonable to shorten it still more, because of inevitable loss of statements confirmations.
3. **Please show and discuss the pathological mechanism of discrepancy between the CT and pathological findings around arteries. Why can EUS show exact condition around the arteries on behalf of CT?**

Encasement of the artery may be due to: 1) tumour extension, 2) fibrosis following down staging radiation or chemoradiotherapy, 3) inflammation as a result of pancreatitis (for example following biliary drainage). Anyway this is the reason for radical surgery denial. We have no patients after chemoradiation or radiation therapy. All the CTs were performed before stenting and there were no cases of prominent pancreatitis confirmed at surgery.

Nevertheless, although the encasement in all the cases was caused by tumor infiltration of periarterial tissues, *in our opinion* US (especially at short distance) has an advantage over CT in evaluation of inflammatory component of infiltration which can constitute that “plane” between the tumor and artery. Of course, it is our supposition, which is to be proven by further investigations.

Reviewer 2

Major:

- 1) The authors insisted “Arterial encasement on CT does not necessarily signify arterial invasion. Whenever PC is considered unresectable endoUS should be used.” They focused on the false-positive or false-negative CT findings to diagnose the arterial invasion of the PDAC. This is interesting study (in my mind), however, we want to know the relationship between the CT findings and pathological findings in detail (perineural invasion, vascular invasion, etc.). Moreover, we need to know the sensitivity and specificity of the diagnosis of the PDAC in both CT and EUS in this study.
- 2) The authors did not mention chemotherapy after surgery. Recently, adjuvant chemotherapy for PDAC is recommended. What is the policy regarding the adjuvant chemotherapy in this institution?
- 3) The authors mentioned “In Group B palliative PDs were undertaken as motivated by the equivocal CT findings regarding the tumor resectability and the surgeon- disclosed SMA and/or CA tumoral involvement after the gland transection, that is, after having crossed “the point of no return”.” Regarding the “the point of no return”, there are some methods which enable to disclose SMA and/or CA tumoral involvement before the transaction of the pancreatic parenchyma. This point should be discussed.

Minor:

- 1) In patients and methods section, Group A was not described.
- 2) Table 1. ChT should be explained.
- 3) In discussion section, too long.

Major points

1. ...we want to know the relationship between the CT findings and pathological findings in detail (perineural invasion, vascular invasion, etc.)

The resection considered radical if there were no tumor cells on frozen section examination in the left resection margins for pancreaticoduodenectomy and in the right margins for distal pancreatectomy (from the text). Case 11 is a pictorial illustration of this topic.

The histological data were the following

Histology	PDAC location	Artery involved on CT	ChT	DFS (mo)	Survival (mo)
1. Tumor cells were detected in the periarterial nerve plexus to the left and to the front of the rRHA, the right and lower sides of the plexus was visibly infiltrated but free of tumor. Artery was definitely uninvolved. (Fig.5 of the main text)	Head	rRHA	+	17	19
2. Tumor cells were detected in the periarterial nerve plexus to the left of the SMA, the right side of the plexus was free of tumor. Artery was definitely uninvolved. (Fig for Case 2(attached))	Body	SMA	+	20	27
3. Tumor cells were detected in the periarterial nerve plexus to the left of the SMA, the right side of the plexus was free of tumor. Artery was definitely uninvolved. (The photo is blurred and omitted).	Body	SMA	+	19	22
4. Tumor cells were detected in the periarterial nerve plexus to the right and to the left of the SMA but artery was definitely uninvolved. (Fig.4 of the main text). After excision of the periarterial plexus the IO biopsy to the left of the SMA was negative.	Head	SMA	+	17	20*
5. Tumor cells were detected in the periarterial nerve plexus lower to the CHA, the left side of the plexus was free of tumor. Artery was definitely uninvolved. (Fig for Case 5 (attached)) The biopsy from the front wall of the portal vein (PV) has revealed tumor negative fibrotic tissue.	Total	CHA	-	12	14
6. Tumor cells were detected in the periarterial nerve plexus to the right of the SMA, the left side of the	Head	SMA + SMA ^v	+	NA	12*

plexus was free of tumor. The inferior pancreaticoduodenal artery was invaded but the SMA itself was definitely uninvolved (Fig.3 of the main text).					
7. Thorough description of the case is presented in figure legend (fig. 2 of the main text). P.S. At the moment patient alive and free of tumor 15 months after surgery.	Body	CA and LHA	+	11	11*
8. Tumor cells were detected in the periarterial nerve plexus to the right of the SMA, the left side of the plexus was free of tumor. Artery was definitely uninvolved. (The photo is blurred and omitted).	Head	SMA	+	NA	8*
9. Tumor cells were detected in the periarterial nerve plexus to the right of the GDA, the right side of the plexus was free of tumor. Artery was definitely uninvolved. (Figs for case 9 (attached).	Body	GDA	-	6	8
10. Tumor cells were detected in the periarterial nerve plexus to the left of the SMA, the right side of the plexus was free of tumor. Artery was definitely uninvolved. (Fig.1 of the main text)	Body	SMA	+	NA	7*
11. Tumor cells were detected in the periarterial nerve plexus to the right of the SMA and CA, the left side of the plexus was free of tumor for both arteries, which were definitely uninvolved. (Figs. for the case 10 (attached).	Head	SMA and CA	+	NA	7*

*- alive. [√] In case 6 there were two SMA segments involved on CT. ChT – chemotherapy.

Attached pictures (This pictures were not included in the text in order not to overload it).

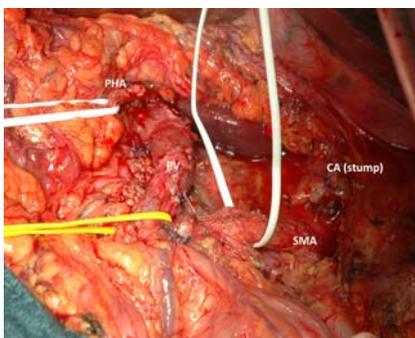


Fig for case 2

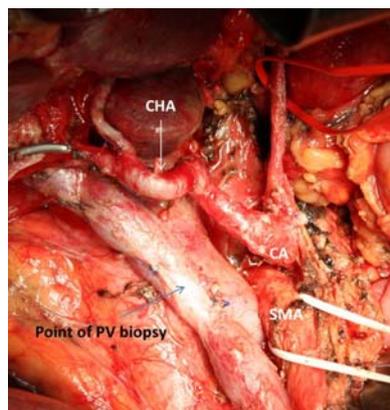


Fig for Case 5

Figs for Case 9

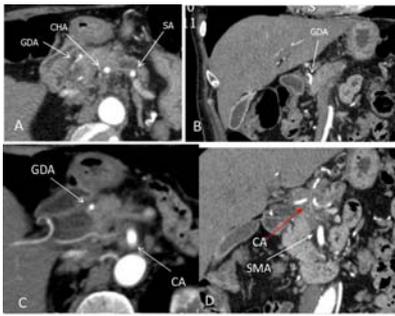
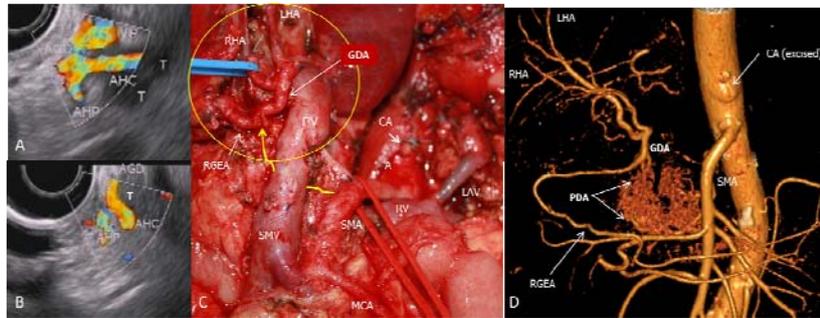
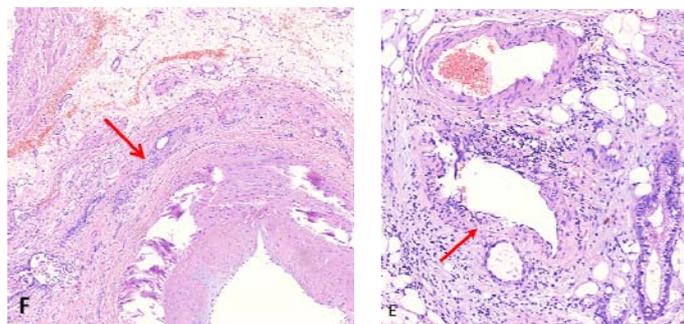


Fig for case 9 Part 1. Preoperative CT. Arterial phase. In this 69-year old woman (case # 9) the pancreatic body cancer was diagnosed by CT with 360° celiac artery (A, D) and 250° gastroduodenal artery (GDA) encasement (A,B,C), which made the case unresectable. a. Axial image. The common hepatic (CHA) and splenic (SA) arteries present circumferential adjacency to pancreatic body ductal adenocarcinoma. The gastroduodenal artery (GDA) appears to be completely encircled by tumor; b. Frontal view. CT evidences circumferential infiltration of GDA; c. The celiac artery (CA) along with CHA springing from it, are completely circumscribed by tumor. D. All three CA branches (red arrow) show circumferential tumor contact. The superior mesenteric artery (SMA) is unaffected.



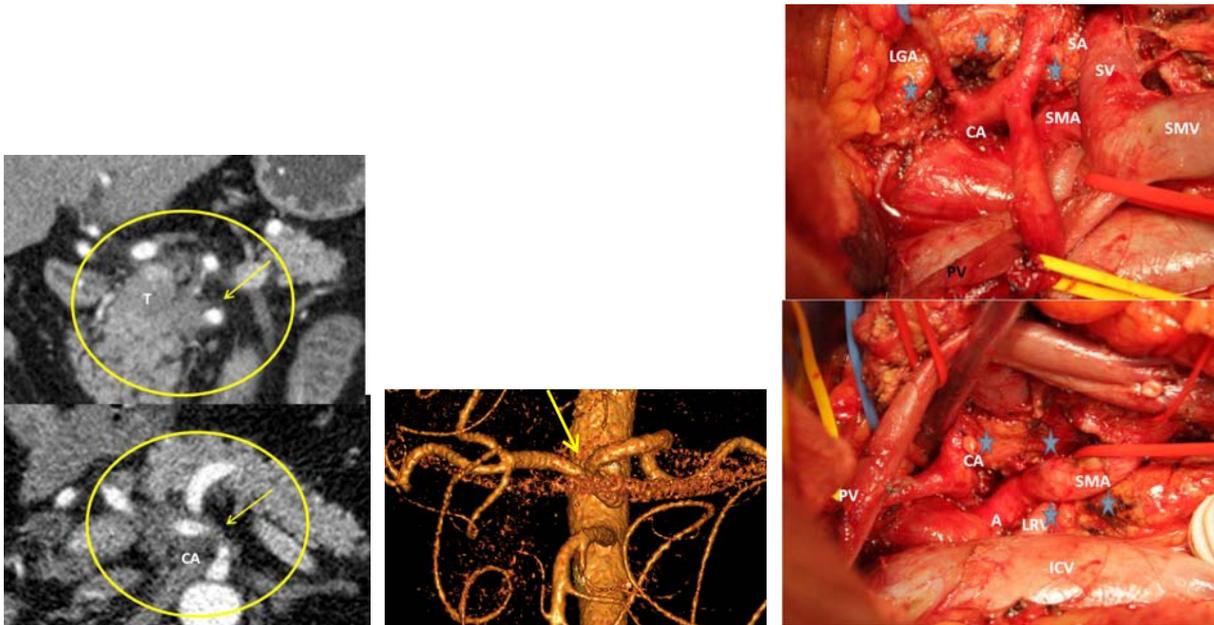
Figures for case 9 Part 2. EndoUS has shown only tumor abutment to gastroduodenal artery (GDA) (A,B); Distal pancreatectomy with excision of the celiac artery (CA) was performed (C). There were no signs of GDA involvement at surgery (C, yellow circle); the 6-month follow-up CT yielded no evidence for disease recurrence and CT angiography displayed quite an ample blood flow in the liver and stomach (D). Yellow curved arrow shows imaginary way of blood flow from the SMA to the GDA after CA excision



The level of resection was R1 because of the contact of the GDA with the tumor (E,F): E. Perivascular tumor growth (cancer cells packages in the small peripancreatic artery adventitia) x 200, H+E; F. Arterial invasion (tumor cells assemblages in CHA adventitia) x 100, H+E;. (For C and D.: A- aorta, SMA – superior mesenteric, CHA – common hepatic, RHA- right hepatic, LHA – left hepatic, RGEA- right gastro-epiploic, MCA- medial colic arteries, PDA- pancreato-duodenal arcade, SMV – superior mesenteric, PV-portal, LRV- left renal, LAV- left adrena veins. For A and B: AHP – arteria hepatica propria, AHC – arteria hepatica communis, AGD – arteria gastroduodenalis, VP – vena porta, T-

tumor.)

Figures for case 11.



Pancreatic head ductal adenocarcinoma 250° SMA and 360° CA encasement on CT with narrowing of CHA on CT and CTA. There were no SMA and CA involvement at surgery. Extended pancreatico-duodenectomy R1 (CA right border). Points of taking biopsy are marked by stars.

P.S. In all the cases of the Group A periarterial neural tissue to the right and to the left of the artery of interest were histologically examined and described but there is no chance to present all of them.

Data of 147 (163 – 16 = 147) patients with PDAC were analysed for arterial involvement. All of them were examined by CT and 87 - by endoUS as well. Sixteen patients were excluded because of distant spread confirmed by CT and at surgery.

Calculations

For CT there were

11 – false-positive + 8- false-negative + 12 true-positive + 116 – true-negative results

Sensitivity = $12 | 12 + 8 = 60\%$; Specificity = $116 | 116 + 11 = 91\%$

For EUS there were

3 - false-negative + 11 - true-positive + 72 – true –negative, 1-false-positive results

Sensitivity = $11 | 11 + 3 = 78.5\%$

Specificity = $72 | 72 + 1 = 98,6\%$

Included in the text.

2. The authors did not mention chemotherapy after surgery. Recently, adjuvant chemotherapy for PDAC is recommended. What is the policy regarding the adjuvant chemotherapy in this institution?

Gemcitabine chemotherapy was a standard postsurgery treatment in pancreatic cancer and

it was performed in 23 cases. Five patients (1 from Group A, 1 from Group B and 3 from group C) refused chemotherapy and in three cases – (1 case from each group) chemotherapy was canceled because of bad physical performance. (It is mentioned in the text + data of tables 1-3). I am sorry: ChT-chemotherapy (included in the text).

3. The authors mentioned “In Group B palliative PDs were undertaken as motivated by the equivocal CT findings regarding the tumor resectability and the surgeon- disclosed SMA and/or CA tumoral involvement after the gland transection, that is, after having crossed “the point of no return”.” Regarding the “the point of no return”, there are some methods which enable to disclose SMA and/or CA tumoral involvement before the transaction of the pancreatic parenchyma. This point should be discussed.

The SMA and CA are situated in the area, access to which can only be achieved after transection of the pancreas representing the point of no return. In our work R2 resections were due to misjudgement regarding resectability in all 8 patients (5.4% of all resections for PDAC). Only one of these eight was operated on by me (EVI) and frankly speaking I feel that false-negative CT data should not become a zero.

Unfortunately I don't know a method which helps to understand involvement/uninvolvement of the SMA or CA before pancreas transection in case of equivocal CT and EUS data on that subject for a large tumour. We tried to use intraoperative US but it turned to be very much US-operator and surgeon- dependent. Having experience of more than 300 Whipples and more than 500 pancreatic resections for different reasons (including multiorgan ones and procedures with vascular resections) I believe now that if you have CT or/and EUS data before surgery saying that arteries are not involved, it means that they are not involved. It depends mainly on surgeon (and/or on some other intraoperative circumstances) what way he/she will go, having in mind that it is easier to say “no” to resection, adding new false-negative result to the statistics. (I have written something about that in Discussion).

The authors in brackets (Koninger J. et al. Biochem Biophys Res Commun 2004; Truty MJ, Urrutia R. Surgery 2007, Bockhorn M, 2009) have described this problem quite well.

Minor points

- 1) **In patients and methods section, Group A was not described** – have been corrected
- 2) **Table 1. ChT should be explained.** CH= chemotherapy
- 3) **In discussion section, too long.**

We discussed your comments with my co-authors and we also feel that Discussion is longer than desirable. At the same time we would like to report the substantiated evidence that was not systematically reported before. Considering that we ought to be accurate and comprehensive. We would like the reader to be certain that the authors master all the fine points and intricacies of the

problem under review with a view to surgeon, radiologist and gastroenterologist, who contributed all to the text. For this reason, in the discussion we could not pass over the following issues:

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The evaluation of the results we have obtained;

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The limitations of resectability assessment in every particular department;

The clinical value of knowing the weak points of CT (as the “gold standard”) in some cases and the typical CT signs of arterial invasion.

The discussion was shorter prior to our communication with 29 of 50 well-known surgeons and radiologists whom we have written on the above mentioned subject. Answering the questions our colleagues raised we have amplified the Discussion to make some points clear (As for example the question of false –negative CT results - R2-resections after crossing of no-return point). That is why we judge it to be critically important to keep the nuances of the discussion as they are.

Reviewer 3

Dear Sir (Madam),

Many more thanks for your thorough studying of our manuscript,

It definitely has led to its improvement. You can find my answers below your questions

This is a fairly well-written paper about a controversial topic. Although it is a small sample set, the authors do a nice job of making some very salient points. I have a few minor comments/suggestions:

- 1. Do all patients get EUS in addition to CT or only those where resectability is in question? This is hinted in the abstract conclusion but not defined in manuscript.**

We have been using EUS systematically from 2008 and during the first year we did both to every patient in order to compare EUS and CT accuracy. In 2009 we have found two first false-positive CT conclusions on behalf of arterial involvement, which were correctly interpreted by EUS. It is this fact that had become the indication for the attempt of radical surgery. By now we have found 11 such cases (described in the manuscript) and are performing EUS to everybody with borderline- or unresectable pancreatic tumors, detected by CT.

- 2. How do the authors reconcile a CT which shows no vessel involvement but EUS suggests vein or artery involvement?**

We actually had got such cases but only 4 (veins) and with description of technical difficulties of EUS. In all the cases the veins were uninvolved but deformed (twisted) at surgery, so we decided to consider such vessels uninvolved.

- 3. How do the authors decide which patients with cT4 disease should be considered for resection? Their algorithm is not clear.**

We consider that true –T4 pancreatic cancer (Stage III) is not a subject for resection. But as you can see from our report, the question is what to consider true- T4. Before the findings described in the manuscript we based our judgment on CT, and now we consider to have as CT so as EUS confirmation of artery(ies) involvement

to sentence the tumor as T4.

4. Is neoadjuvant chemotherapy/chemoradiotherapy ever considered?

There were no cases of preoperative radio- or radiochemotherapy. About chemotherapy it is mentioned in the text (Results) but may be not prominently “Eight patients in Group A, 6 in Group B and 8 in Group C received and/or are receiving gemcitabine chemotherapy. One patient with pancreatic body cancer from Group A was given gemcitabine and eloxatin neoadjuvant chemotherapy.”

May be the best option for the GroupA is the neoajuvant CRT followed by resection but I don't know at the moment. It has to be investigated.

5. Make the title a single declarative statement rather than a 2-sentence question.

Thank you. Corrected. Now it is “Does arterial encasement on CT always mean invasion in pancreatic cancer?”

6. The last paragraph of the introduction is confusion and should be rewritten in more simple terms.

Thank you. Corrected

7. In methods, CT description of "triphasic" refers to the 3 phases of unenhanced, arterial, and portal venous phases not unenhanced + triphasic.

Thank you. Corrected

8. Page 5, last sentence before stats section should read: "...found within 1mm...surface, where..."

Thank you. Corrected

9. Results, 1st paragraph: callout to table 1 actually refers to data (tumor size) listed in table 4.

Thank you very much. The tables were renamed and repositioned.

10. What does ChT mean in the tables?

I am sorry. ChT=chemotherapy. Thank you. Corrected

11. Figures 1-5 will only be worthwhile including if they are high quality and in color. If not, then could use 1 representative case and omit intraoperative pictures.

Absolutly agree. All of them are of high quality and in color. We consider important to demonstrate as much IO pictures as much as sufficient and necessary to show that the event we are writing about is systematic and not anecdotal and how it looks like (This was one of the causes why we have chosen e-journal). We have pictures for every case but some of them were omitted because of lack of space and two of them were blurred.

12. Figure 3, please fix the labels in F (e.g. "VP" should be "PV" and more convential english labeling of hepatic arteries)

Thank you. Corrected.

13. Discussion, 2nd paragraph: 1st sentence is confusing. Please rewrite.

Thank you. Corrected.

14. Page 14, 4th paragraph: should read "...even their combination, were absolutely..."

Thank you so much. Corrected.

15. In the discussion, the authors refer to intraoperative "revision." What does this mean? Visualization? Dissection?

Agree, it is unclear. We have changed this word in the text to “intraoperative exploration, including visualization, palpation and even transection of the pancreas”

16. In general, the discussion can be shortened with fewer references. Instead of citing every reference to support a sentence, include the most relevant or best papers.

I discussed your comments with my co-authors and we also feel that Discussion is longer than

desirable. At the same time we would like to report the substantiated evidence that was not systematically reported before. I think that you will agree with us that the less we talk about something the more it is collected to say about. Considering that we ought to be accurate and comprehensive. We would like the reader to be certain that the authors master all the fine points and intricacies of the problem under review with a view to surgeon, radiologist and gastroenterologist, who contributed all to the text. For this reason, in the discussion we could not pass over the following issues:

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The discussion was shorter prior to our communication with 29 of 50 well-known surgeons and radiologists whom I have written on the above mentioned subject. Answering the questions our colleagues raised we have amplified the Discussion to make some points clear. That is why we judge it to be critically important to keep the nuances of the discussion as they are.

17. The authors often refer to "frontal" imaging on CT. More common description would be "sagittal"

Thank you. Corrected.

Sincerely yours,

Vyacheslav Egorov

Reviewer 4

Dear Sir,

Thank you very much for your thorough studying of our work. We consider all your comments reasonable and improving the manuscript. You will find step by step answers on your comments below.

In their study, the authors were able to identify a group of patients with false-positive CT results of arterial invasion and borderline resectable tumors, who did benefit from pancreatic resection. They state that arterial encasement on CT does not necessarily signify arterial invasion and gave the recommendation that whenever PC is considered unresectable endoscopic ultrasound (EUS) should be used. Furthermore, they found out that a decision regarding irresectability should not be based only on the results of operative revision and palpation and that in selected cases radical resection may provide a survival benefit.

Main Comment

This study is not the first evaluation of CT accuracy for the assessment of arterial invasion in PC. Most studies however focus on inaccurate assessment of resectability due to underestimation of the vascular invasion. In contrast, this study attempts to address the reverse side of the problem by determining overestimation of arterial involvement in patients with PC. Thus, it is a nice piece of work emphasizing the need for a combined use of CT and EUS for the detection of arterial involvement in PC.

The analysis involves a thorough research on 163 well chosen pancreatic resections being performed at the Vishnevsky Institute of Surgery in Moscow, Russia. Using a predefined search strategy, 11 patients with controversial CT and EUS data in regard to arterial invasion after R0/R1 procedures (false-positive CT results) were identified and compared to survival after 8 R2 resections (false-negative CT results) as well as 12 bypass procedures for locally advanced cancer (true-positive CT results).

Accordingly, the authors conclude that false-positive CT evaluation does overestimate the extent of arterial involvement and that EUS should be used in order to confirm CT results. Furthermore, this study gives evidence that radical resection may be possible in selected cases and provide survival benefit.

Although these results are quite interesting, there are a few deficiencies in the manuscript, which preclude adequate and full interpretation of these data. These flaws do compromise the results and the authors' evaluation with respect to the role of the recommended surgical approach:

1. Regarding the survival data in figure 6 the expected median survival has not been reached because more than half of patients in group A were alive at the last follow-up. Since the end of follow-up period for the patients alive was in July 2012, the study should be updated again before publication in order to affirm the results using the newest survival data.

We have updated the results and it looks like this (below) for group A by the middle of December 2012. Some patients live in remote regions and we couldn't get information about their DFS.

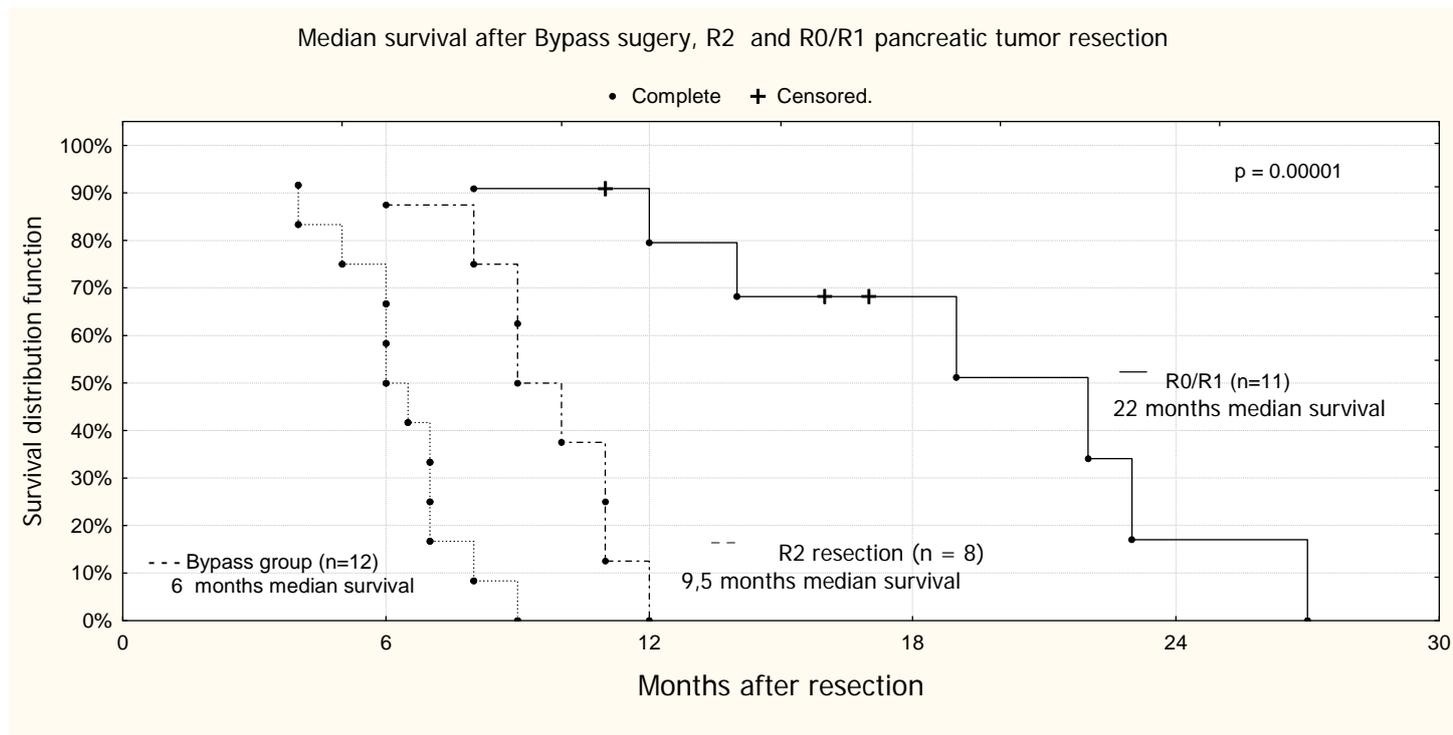
Table 2 (new). Group A. Characteristics of the patients who underwent radical (R0-1) surgery for PDAC with circular arterial involvement on CT.

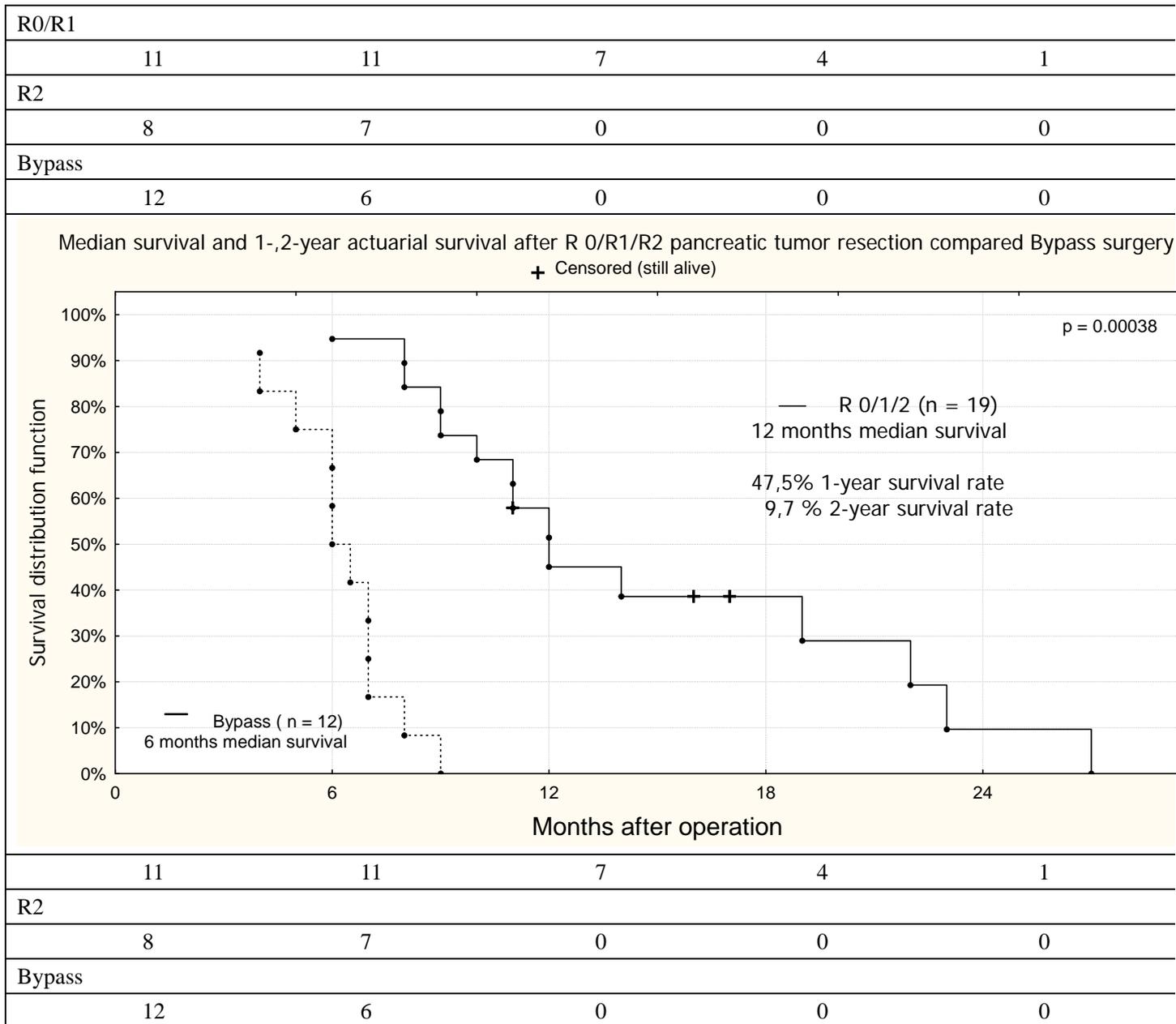
N	Stage R factor		PDAC location	Artery involved on CT	ChT	DFS (mo)	Survival (mo)
1	cT4NxM0	pT3N1M0(R1)	Head	rRHA	+	17	19
2	cT4NxM0	pT3N1M0(R1)	Body	SMA	+	20	27
3	cT4NxM0	pT3N1M0(R1)	Body	SMA	+	19	22
4	cT4N1M0	pT3N1M0(R1)	Head	SMA	+	17	23
5	cT4NxM0	pT3N0M0 (R1)	Total	CHA	-	12	14
6	cT4NxM0	pT3N1M0(R1)	Head	SMA + SMA [√]	+	NA	17*
7	cT4N1M0	pT2N0M0 (R0)	Body	CA and LHA	+	16	16*
8	cT4N1M0	pT3N1M0(R1)	Head	SMA	+	10	12
9	cT4N1M0	pT3N1M0(R1)	Body	GDA	-	6	8
10	cT4NxM0	pT4N1M0(R1)	Body	SMA	+	NA	11*
11	cT4N1M0	pT3N1M0(R1)	Head	SMA and CA	+	10	11*

* - alive. [√] In case 6 there were two SMA segments involved on CT.

There were significant differences in survival between the groups ($p = 0.0001$). The one-year survival was not attained in Groups B and C, notwithstanding the fact that the difference in survival between Groups B and C was considerable ($p = 0.003$). The median survival for Group B was 9.5 months (95%CI: 8,5 – 11 mo). The one-year survival rate in Group A was 79,5% (95%CI: 54,5% – 100%), two-year – 17% (95%CI: 0 – 47,5%) with a median follow-up period of 16 months (95%CI: 11 – 22 mo) and median survival of 22 months (95% CI: 14 - 23 months). The difference in survival between groups A and B was significant ($p_{\log_{\text{rank}}} = 0.00001$) (Fig.6). The actuarial one-year survival in united resection group (Group A + Group B), i.e., in resections nonmettering factor R, was as high as 45% (95%CI: 21% – 68%), two-year – 9,7% (95%CI: 0 – 27,5%) with median survival of 12 months (95%CI: 10 – 22 mo). The median survival following palliative operations was 6 months (95%CI: 5 – 7 mo) and there were significant differences in survival between the groups (Fig.7).

The corresponding changes were included in the main text and in Figs. 6 and 7.





2. Throughout the whole text there are spelling and grammatical errors that disturb the article’s informative value. Accordingly, some statements need revision including the following: “We consider resection as R0 if there were no tumor cells found within ≥ 1 mm distance from the specimen circumferential margins except anterior surface, were “0-mm rule” worked.” or “Photograph of operating field after distal pancreatectomy R0 with excision of the celiac (CA), common (CHA), left gastric (LGA), and left hepatic artery (LHA) and resection of gastroduodenal artery (GDA) was performed and the were no major arteries involvement was identified at surgery and histopathology“.

The text was corrected and the following was included in the manuscript:

“We consider resection as R0 if there were no tumor cells found within 1 mm distance from the specimen circumferential margins except for the anterior surface evaluation applying the “0 mm clearance” rule.”

“Photograph of operating field after distal pancreatectomy (R0 resection) with excision of celiac, common,

left gastric, left hepatic arteries and gastroduodenal artery resection in the absence of any evidence for major arterial invasion either at surgery or on histopathology”

3. The authors should rephrase the manuscript title “Does arterial encasement on CT always mean invasion at surgery in pancreatic cancer? If not, how can we assess resectability and what is the strategy?” in order to clarify the aim and results of the study, e.g. “CT-based diagnostic is insufficient in the...”

We consider that new title “**CT-based diagnostics may be insufficient in pancreatic cancer unresectability determination**” reflects the idea better.

Sincerely grateful for your work, Vyacheslav Egorov

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastrointestinal Surgery*/

Sincerely yours,



Sincerely,

Egorov Viacheslav Ivanovich, MD, PhD,

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