

1     **Systematic evaluation of radiological findings in the assessment of resectability of peri-**  
2             **ampullary cancer by CT using different contrast phase protocols**

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**Abstract**

Aims: To determine the relative significance of radiological signs in determining the resectability of peri-ampullary cancer (PC) and to assess the value of multi-phase imaging in detecting these findings.

Materials and Methods: Blinded, double re-reporting of pre-operative imaging from five hospitals was undertaken of 411 patients undergoing surgery for PC over an eight year period, of whom 119 patients were found to be inoperable at the time of surgery.

Results: The median tumour size was 26.7 mm and the proportion of patients reported to have regional lymphadenopathy (RL), venous (VI) and arterial involvement (AI) was 24.7%, 11.5% and 3.9% respectively and was similar regardless of the number of contrast phases undertaken. Significant associations were however noted between individual risk factors: VI was closely associated with tumour size ( $p=0.002$ ) and AI ( $p< 0.0001$ ). In multi-variable analysis AI, VI and RL were independently associated with resectability (relative risk of resection =0.05, 0.31 and 0.51 respectively). Tumour size however was not associated with resectability when VI was included in the multivariate model.

53 Conclusions: The use of multiple vascular contrast phases has no measureable impact on the  
54 rate of determination of tumour resectability of PC. In pre-operative staging AI is the most  
55 significant adverse finding for resectability. Large tumour diameter is not an adverse finding  
56 in isolation from other risk factors.

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60 **Key words**

61 Ampulla, Bile duct, Cancer, CT scan, Pancreas

62

63 **Abbreviations and acronyms**

64 AI: Arterial involvement

65 PC: Peri-ampullary cancer

66 RL: Regional lymphadenopathy

67 VI: Venous involvement

68

69 **Introduction**

70 Determination of tumour resectability is a major aspect of the interpretation of pre-operative  
71 imaging of peri-ampullary cancer (PC). The findings of distant metastases and local invasion  
72 resulting in occlusion of major arteries or veins are contraindications to attempted surgical  
73 resection, whereas lesser degrees of arterial involvement (AI) and venous involvement (VI),  
74 including abutment and tapering, are relative contraindications, as imaging can sometimes be  
75 inaccurate in determining these findings (1-4), and vein resection can be undertaken where  
76 incomplete venous occlusion is noted (5-7). Tumour size (8) and regional lymphadenopathy  
77 (RL) (9, 10) have also been shown to be associated with unresectability, although RL is a  
78 relative contraindication as these nodes are removed as part of a Whipple procedure (11).  
79 This finding may however be a surrogate marker of an aggressive malignancy, which will  
80 progress rapidly to become inoperable.

81 Despite pre-operative imaging to exclude patients with contraindications to surgery a  
82 proportion of patients with PC proceeding to operation are found to be inoperable, either due  
83 to unresectable invasion of vascular structures or the presence of metastatic disease. This may  
84 result from either understaging by CT or rapid tumour progression in the interval between  
85 imaging and surgery.

86 Pre-operative staging of PC is commonly undertaken by contrast-enhanced CT scan. Some  
87 authorities recommend tri-phasic imaging (12), including pre-contrast phase, arterial phase  
88 and portal phase, although the benefits of this over monophasic scans (portal venous phase  
89 only) and biphasic scans (arterial and portal phases) have not been demonstrated. This has  
90 implications in terms of radiation exposure and resource utilisation. There have also been  
91 major improvements in CT scan technology in recent years with the development of multi-

92 detector imaging (13), which would be expected to lead to a reduction in the proportion of  
93 false negative findings, and may have reduced the need for multi-phase imaging.

94 The principal study aim is to determine a hierarchy of radiological findings in predicting the  
95 resectability of PC in patients undergoing surgery at a regional centre within a Cancer  
96 Network serving five hospitals (A-E) and to investigate the cause of unresectability (local  
97 invasion or metastatic disease) associated with these findings. Secondary aims were to  
98 explore the effect of varied imaging protocols in the detection of these findings to determine  
99 potential advantages of multi-phase imaging in clinical practice.

## 100 **Material and Methods**

101 Details of consecutive patients undergoing surgical exploration for suspected PC between  
102 January 2006 and January 2014 were collected in a prospective database. Patients were  
103 offered surgery following review of imaging at a specialist HPB MDT and all scans were  
104 performed on 64-slice multi-detector CT (MDCT). Relevant abdominal CT scans were  
105 retrieved from referring hospitals, anonymised and uploaded to a dedicated research hard-  
106 drive. Images were then re-reported independently by two radiologists with higher training in  
107 pancreato-biliary imaging using standard criteria(14). The number of vascular contrast  
108 phases was recorded for each patient and the proportion of patients having mono, bi and tri-  
109 phasic imaging in each of the referring hospitals was determined, along with the association  
110 of the number of scan phases with the main radiological findings. Specific data fields were  
111 created to collect information relating to hospital of origin, the presence of a biliary stent  
112 inserted at ERCP, tumour size, regional nodal status (presence of lymph nodes >1cm in  
113 transverse diameter) and vascular involvement status. Radiological evidence of arterial and  
114 venous involvement were defined according to published criteria (14) (Figure 1). In the  
115 assessment of a binary variable (e.g. nodal status) a positive outcome was recorded only

116 when both radiologists agreed on the finding. For tumour size the mean of the two findings  
117 was taken.

118 At surgery initially a search for metastatic disease was undertaken before an attempt at  
119 dissection of the primary tumour. The tumour was considered to be unresectable due to local  
120 invasion when the operating surgeon was unable to resect the tumour after trial dissection  
121 without undertaking arterial resection or where there was occlusion or extensive invasion of  
122 the portal or superior mesenteric vein. Data retrieved from the database included the  
123 operative finding of either unexpected distant metastases or local invasion by tumour into  
124 vascular structures. The proportion of resectable tumours was recorded for consecutive  
125 quartiles (two year intervals) of the study period. To explore further the predictive value of  
126 radiological findings the operative outcome among patients where the tumours were found to  
127 be unresectable were categorised into the finding of metastatic disease or local invasion.

128 Discrete variables and interdependence of radiological findings were analysed by Chi-square  
129 test and continuous variables by Mann-Whitney. Estimates of the relative value of  
130 radiological parameters in the prediction of resectability of PC were determined by logistic  
131 regression analysis.

132 Ethical approval for the study was obtained from the South West Health Research Authority  
133 Research Ethics Committees. No patient consent was required for this study because patient  
134 data were collected in the course of normal hospital care and were anonymised for research  
135 purposes.

136 The study is registered with ClinicalTrials.gov (unique identifier NCT02296736).

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139 **Results**

140 Operative details and relevant pre-operative imaging were available in 409 patients (Figure  
141 2), of median age 66.9 (28-86) years, of whom 55.8% were male. The median age (66.7 v  
142 67.5 years), percentage of male patients (54.5% v 59.8%) and median interval between  
143 imaging and surgery (42 v 39 days,  $p=0.419$ ) did not differ between patients proceeding to  
144 resection and those where the lesion was found to be unresectable.

145 Analysis of images revealed a similar proportion of mono-, bi- and tri-phasic scans. There  
146 was variation in the number of vascular contrast phases undertaken in scans from different  
147 hospitals; however the rate of detection of the main radiological end-points did not differ  
148 according to the number of contrast phases undertaken (Table 1). In particular the proportion  
149 of patients noted to have AI did not differ between patients where only portal venous imaging  
150 was performed (3 of 134) and those where additional arterial phase imaging (bi- and tri-  
151 phasic scans) was also performed (13 of 275) ( $p=0.223$ ). The primary tumour was visible in  
152 250 patients (61.1%), with no difference in the rate of detection in patients having different  
153 contrast phase protocols (Table 1). Similarly the median tumour size was 26.7 (8-70) mm and  
154 did not differ between patients having different scan phases ( $p= 0.39$ ). Where a tumour was  
155 visible RL, VI and AI were noted in 101 (40.4%), 47 (18.8%) and 16 (6.4%) of patients  
156 respectively. Among the 159 patients where no primary tumour was visible, RL was noted in  
157 40 (25%) patients. Tumour size was noted to be greater in patients with RL (28.5mm v  
158 26mm), AI (30.7mm v 26.5mm) and VI (33mm v 25.5mm) than in those without these  
159 findings ( $p= 0.02$ ,  $0.03$  and  $0.0001$  respectively). In evaluation of interdependence of pre-  
160 operative risk factors VI was noted to be strongly associated with AI ( $p=0.000$ ). Of the 16  
161 patients with AI, 8 (50%) also were noted to have VI. The finding of RL was not significantly  
162 associated with either AI ( $p=0.472$ ) or VI ( $p=0.108$ ).

163 Biliary stents had been inserted prior to CT scan in 73 (17.8%) patients. The proportion of  
164 patients with radiologically detectable RL did not differ between those who had (17/72,  
165 23.6%) and those who had not (84/337, 25%) had a stent inserted prior to CT scan ( $p=0.814$ ).

166 Surgical resection of the PC was completed in 292 patients (71.4%). Resection was  
167 completed more commonly among the 159 patients where no lesion was visible (126, 79%)  
168 than among the 250 patients where the tumour was visible (166, 66.4%) ( $p=0.005$ ). Among  
169 the 155 patients with a visible tumour and no adverse risk factors (RL, AI or VI) on pre-  
170 operative imaging, the median tumour size did not differ between the 121 patients where the  
171 tumour was resectable (24.5 mm, IQR 20.5-30.42) and the 34 patients where the tumour was  
172 not resectable (26.7mm, IQR 20-28.5mm) ( $p=0.55$ ).

173 Of the 17 patients with VI on pre-operative imaging where resection was completed, partial  
174 venous resection was necessary in three (17.6%) patients. Vein resection was also required in  
175 five of the 348 patients (1.4%) where VI was not noted pre-operatively.

176 The final pathological diagnosis of resected specimens is shown in Table 2.

177 In univariate analysis the presence of a visible tumour, tumour size, RL, AI and VI on pre-  
178 operative imaging were all associated with unresectability of the tumour (Table 3). However  
179 in multivariate analysis the strongest association with tumour resectability was with the  
180 presence of AI (Table 3). Tumour size and VI were found to be mutually exclusive for  
181 significance in the multi-variate model.

182 In the 117 patients where the tumour was not resected this was due to the finding of hepatic  
183 metastatic disease in 45 patients (37.8%) or local invasion of vascular structures in 72  
184 patients (60.5%). The proportion of patients with unresectable disease was 16/67 (23.8%),  
185 35/93 (37.6%), 32/119 (26.2%) and 34/130 (26.1%) ( $p=0.17$ ) in consecutive time quartiles of



186 the study. No difference was noted in the reasons for unresectability (local invasion or  
187 metastatic disease) among patients with different pre-operative radiological findings (Table  
188 4).

189

## 190 **Discussion**

191 This study allows the determination of a hierarchy of relative contraindications to resection of  
192 peri-ampullary cancer, based on a systematic assessment of radiological findings. In  
193 multivariable analysis the likelihood of completing surgical resection was reduced by a factor  
194 of 0.05, 0.31 and 0.51 by a finding of AI, VI and RL respectively, compared to a patient with  
195 none of these findings. In the absence of these findings tumour size was not associated with  
196 resectability. The study also revealed significant interdependence of radiological signs, with  
197 VI closely associated with tumour size ( $p < 0.0001$ ) and with AI ( $p = 0.000$ ). The study  
198 demonstrated that the proportion of patients with unresectable disease at the time of surgery  
199 has not declined over the eight year period of the study, and that the radiological findings are  
200 similar regardless of the number of scan phases undertaken. In addition pre-operative  
201 radiological findings were not able to predict the reason the pancreatic tumour was not  
202 resectable at the time of surgery (metastatic disease or local progression).

203 Many studies have shown that AI and VI are risk factors for non-resection of pancreatic  
204 tumours (15-17). Most have focussed on assessing the accuracy of MDCT in identifying  
205 these risk factors in comparison with operative findings or histology (18-20). This study has  
206 used a structured reporting protocol to assess the relative risk that pre-operative identification  
207 of these findings entails for individual patients in terms of tumour resectability. AI is shown  
208 to be the most significant adverse finding, with a relative risk of resection of 0.05 compared  
209 to a patient without this finding. This may be due to the hepatic and superior mesenteric

210 arteries lying further from the duodenal ampulla than venous structures, denoting a greater  
211 degree of invasion. The observation that the radiological findings of AI and VI are associated  
212 with each other may also reflect the spatial relationship of these structures, with VI occurring  
213 first followed by AI.

214 The significance of radiological evidence of RL has been less well investigated previously. It  
215 is interesting to note that the presence of RL was not influenced by the insertion of biliary  
216 stents, so this finding should be attributed to a malignant, rather than inflammatory process.  
217 RL was also not associated with other signs of local tumour progression, and is only weakly  
218 associated with primary tumour size. The development of lymph node metastases in PC may  
219 therefore depend on different biological processes to primary tumour enlargement and local  
220 invasion. RL was however independently associated with tumour unresectability. This is  
221 probably due to this finding being a marker of a more aggressive malignancy. In a large  
222 proportion (69%) of patients with RL however the tumour remains resectable at surgery.

223 Our study confirms that although tumour size is associated with invasion of vascular  
224 structures, size alone does not lead to an increased risk of non-resection in the absence of  
225 other adverse findings. This is significant as some centres have used tumour size alone as a  
226 factor in the decision to offer surgery for PC(8).

227 The observation that 20% of patients with no detectable tumour radiologically are found to be  
228 inoperable at the time of surgery is an interesting finding. This suggests that although the  
229 interval from imaging to surgery has only a small impact on resectability in large series(21)  
230 there may be a more aggressive subset where progression proceeds rapidly. Similarly among  
231 the 271 patients where no adverse radiological signs were identified 54 (19.9%) were still  
232 found to be inoperable at the time of surgery. Caution must be exercised therefore in the  
233 interpretation of radiological findings when counselling patients. In addition although vein

234 resection was required in 17.6% of patients undergoing resection where VI was noted on pre-  
235 operative imaging it was also necessary in 1.4% of cases without VI on pre-operative  
236 imaging. These observations emphasize the limitations of pre-operative imaging in planning  
237 surgery for PC.

238 The weaknesses of this study mainly relate to the non-standardised imaging protocols  
239 undertaken in different centres, and its retrospective nature. This study however represents an  
240 analysis of the value of pre-operative imaging in routine clinical practice, rather than under  
241 trial conditions, and the results are therefore likely to be relevant to other centres undertaking  
242 this type of surgery. Of particular interest is the finding that the radiological findings and  
243 resection rate are similar regardless of the number of contrast phases. Although multi-phase  
244 pancreatic-protocol CT is considered the 'gold-standard' in assessing resectability of PC(12),  
245 our results indicate that the resectability rate is unaltered by the CT technique used. It is  
246 possible that with a larger study the use of arterial phase contrast may lead to greater  
247 sensitivity in the detection of AI. This however does not seem necessary in patients with  
248 small tumours and no evidence of VI, where the risk of AI is very low. The study is also  
249 limited by the number of radiologists undertaking rereporting (two). The agreement between  
250 radiologists is being addressed separately and it is possible that the results have been biased  
251 by individual radiologists performance.

252 The analysis of surgical outcomes has revealed the most common cause for non-resection  
253 was invasion of vascular structures (60.5%), with metastatic disease a less common finding  
254 (37.8%). Patients noted to have AI or VI on pre-operative imaging had a similar likelihood of  
255 being inoperable due to metastatic disease or local invasion at the time of surgery, suggesting  
256 that these findings are markers of aggressive malignancy. CT has a high resolution for  
257 hepatic metastases, which has increased in recent years(22). Despite this the proportion of  
258 patients with unresectable disease has remained largely unchanged over the period of study.

259 This finding suggests that disease progression between imaging and the time of surgery may  
260 be a more significant cause of inoperability than understaging by CT. There may therefore be  
261 an irreducible number of patients with rapidly progressive disease who will be unresectable at  
262 the time of surgery, regardless of the quality of the imaging and reporting undertaken.

263 The strength of this study lies in its large size and in the assessment of imaging of  
264 heterogeneous technique from different hospitals. Other studies have shown similar risk  
265 factors for non-resection(23, 24), and a similar rate of non-resection (23, 24) at the time of  
266 surgery, and there is little available evidence that this rate has declined with improved  
267 imaging. This may be due to alterations in the threshold for undertaking surgery in borderline  
268 cases and improvements in surgical technique. The study however reveals significant  
269 limitations in the ability of MDCT to predict the presence of surgically significant operative  
270 findings.

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272 The authors declare no conflict of interest

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283 **References**

284

- 285 1. Marinelli T, Filippone A, Tavano F, Fontana A, Pellegrini F, Koninger J, et al. A  
286 tumour score with multidetector spiral CT for venous infiltration in pancreatic cancer:  
287 influence on borderline resectable. *La Radiologia medica*. 2014;119(5):334-42. Epub  
288 2014/03/13.
- 289 2. Egorov VI, Petrov RV, Solodinina EN, Karmazanovsky GG, Starostina NS,  
290 Kuruschkina NA. Computed tomography-based diagnostics might be insufficient in the  
291 determination of pancreatic cancer unresectability. *World journal of gastrointestinal surgery*.  
292 2013;5(4):83-96. Epub 2013/05/30.
- 293 3. Zhang Y, Huang J, Chen M, Jiao LR. Preoperative vascular evaluation with computed  
294 tomography and magnetic resonance imaging for pancreatic cancer: A meta-analysis.  
295 *Pancreatology : official journal of the International Association of Pancreatology*.  
296 2012;12(3):227-33.
- 297 4. Andersen HB, Effersoe H, Tjalve E, Burcharth F. CT for assessment of pancreatic and  
298 periampullary cancer. *Acta radiologica*. 1993;34(6):569-72.
- 299 5. Howard TJ, Villanustre N, Moore SA, DeWitt J, LeBlanc J, Maglinte D, et al.  
300 Efficacy of venous reconstruction in patients with adenocarcinoma of the pancreatic head.  
301 *Journal of gastrointestinal surgery : official journal of the Society for Surgery of the*  
302 *Alimentary Tract*. 2003;7(8):1089-95. Epub 2003/12/17.
- 303 6. Capussotti L, Massucco P, Ribero D, Viganò L, Muratore A, Calgaro M. Extended  
304 lymphadenectomy and vein resection for pancreatic head cancer: outcomes and implications  
305 for therapy. *Archives of surgery*. 2003;138(12):1316-22. Epub 2003/12/10.
- 306 7. van Geenen RC, ten Kate FJ, de Wit LT, van Gulik TM, Obertop H, Gouma DJ.  
307 Segmental resection and wedge excision of the portal or superior mesenteric vein during  
308 pancreatoduodenectomy. *Surgery*. 2001;129(2):158-63. Epub 2001/02/15.
- 309 8. Garcea G, Dennison AR, Pattenden CJ, Neal CP, Sutton CD, Berry DP. Survival  
310 following curative resection for pancreatic ductal adenocarcinoma. A systematic review of  
311 the literature. *JOP : Journal of the pancreas*. 2008;9(2):99-132. Epub 2008/03/11.
- 312 9. Jeffrey RB. Pancreatic cancer: radiologic imaging. *Gastroenterology clinics of North*  
313 *America*. 2012;41(1):159-77. Epub 2012/02/22.
- 314 10. Maithel SK, Khalili K, Dixon E, Guindi M, Callery MP, Cattral MS, et al. Impact of  
315 regional lymph node evaluation in staging patients with periampullary tumors. *Annals of*  
316 *surgical oncology*. 2007;14(1):202-10.
- 317 11. Pedrazzoli S, DiCarlo V, Dionigi R, Mosca F, Pederzoli P, Pasquali C, et al. Standard  
318 versus extended lymphadenectomy associated with pancreatoduodenectomy in the surgical  
319 treatment of adenocarcinoma of the head of the pancreas: a multicenter, prospective,  
320 randomized study. Lymphadenectomy Study Group. *Annals of surgery*. 1998;228(4):508-17.  
321 Epub 1998/10/28.
- 322 12. Fletcher JG, Wiersema MJ, Farrell MA, Fidler JL, Burgart LJ, Koyama T, et al.  
323 Pancreatic malignancy: value of arterial, pancreatic, and hepatic phase imaging with multi-  
324 detector row CT. *Radiology*. 2003;229(1):81-90. Epub 2003/10/02.
- 325 13. Satoi S, Yanagimoto H, Toyokawa H, Tanigawa N, Komemushi A, Matsui Y, et al.  
326 Pre-operative patient selection of pancreatic cancer patients by multi-detector row CT.  
327 *Hepato-gastroenterology*. 2009;56(90):529-34. Epub 2009/07/08.
- 328 14. Al-Hawary MM, Francis IR, Chari ST, Fishman EK, Hough DM, Lu DS, et al.  
329 Pancreatic ductal adenocarcinoma radiology reporting template: consensus statement of the

- 330 Society of Abdominal Radiology and the American Pancreatic Association. *Radiology*.  
331 2014;270(1):248-60. Epub 2013/12/21.
- 332 15. Lu DS, Reber HA, Krasny RM, Kadell BM, Sayre J. Local staging of pancreatic  
333 cancer: criteria for unresectability of major vessels as revealed by pancreatic-phase, thin-  
334 section helical CT. *AJR*. 1997;168(6):1439-43.
- 335 16. Edge SB, Carolyn CC. The American Joint Committee on Cancer: the 7th Edition of  
336 the AJCC Cancer Staging Manual and the Future of TNM. *Annals of surgical oncology*.  
337 2014;17:1471-4.
- 338 17. Tempero MA, Arnoletti JP, Behrman SW, Ben-Josef E, Benson AB, 3rd, Casper ES,  
339 et al. Pancreatic Adenocarcinoma, version 2.2012: featured updates to the NCCN Guidelines.  
340 *Journal of the National Comprehensive Cancer Network : JNCCN*. 2012;10(6):703-13. Epub  
341 2012/06/09.
- 342 18. Khattab EM, AlAzzazy MZ, El Fiki IM, Morsy MM. Resectability of pancreatic  
343 tumors: Correlation of multidetector CT with surgical and pathologic results. *The Egyptian*  
344 *Journal of Radiology and Nuclear Medicine*. 2012;43(1):11-7.
- 345 19. Valls C, Andía E, Sanchez A, Fabregat J, Pozuelo O, Quintero JC, et al. Dual-Phase  
346 Helical CT of Pancreatic Adenocarcinoma. *American Journal of Roentgenology*.  
347 2002;178(4):821-6.
- 348 20. Takeshita K, Kutomi K, Haruyama T, Watanabe A, Furui S, Fukushima J, et al.  
349 Imaging of early pancreatic cancer on multidetector row helical computed tomography. *The*  
350 *British journal of radiology*. 2010;83(994):823-30. Epub 2010/05/06.
- 351 21. Amr B, Shahtahmassebi G, Briggs CD, Bowles MJ, Aroori S, Stell DA. Assessment  
352 of the effect of interval from presentation to surgery on outcome in patients with peri-  
353 ampullary malignancy. *HPB*. 2016;18(4):354-9.
- 354 22. Takamori H, Ikeda O, Kanemitsu K, Tsuji T, Chikamoto A, Kusano S, et al.  
355 Preoperative detection of liver metastases secondary to pancreatic cancer: utility of combined  
356 helical computed tomography during arterial portography with biphasic computed  
357 tomography-assisted hepatic arteriography. *Pancreas*. 2004;29(3):188-92. Epub 2004/09/16.
- 358 23. Shaib Y, Davila J, Naumann C, El-Serag H. The impact of curative intent surgery on  
359 the survival of pancreatic cancer patients: a U.S. Population-based study. *The American*  
360 *journal of gastroenterology*. 2007;102(7):1377-82. Epub 2007/04/04.
- 361 24. Neoptolemos JP, Stocken DD, Friess H, Bassi C, Dunn JA, Hickey H, et al. A  
362 randomized trial of chemoradiotherapy and chemotherapy after resection of pancreatic  
363 cancer. *The New England journal of medicine*. 2004;350(12):1200-10. Epub 2004/03/19.

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379 findings

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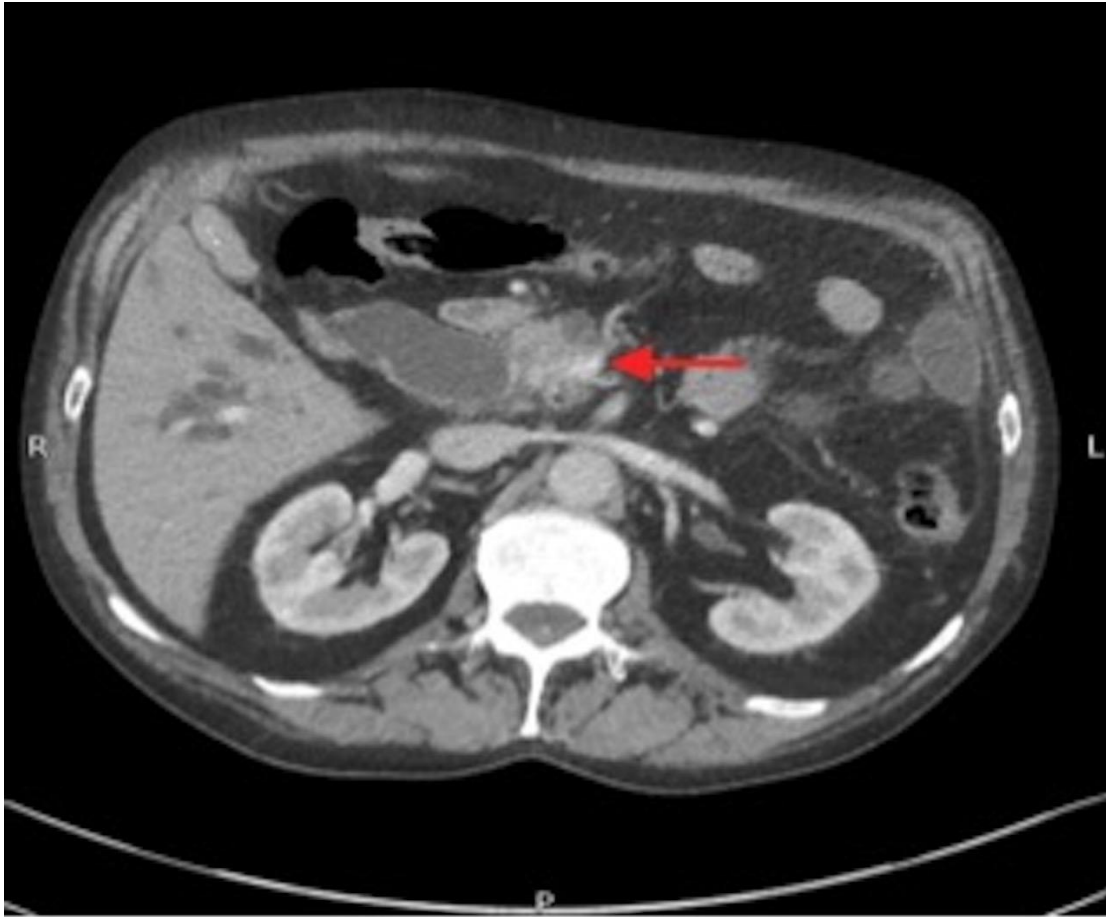


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383 Figure 1-a. MDCT imaging demonstrating SMA involvement by PC (Arrow)

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386 Figure 1-b. MDCT imaging demonstrating SMV involvement by PC (Arrow)

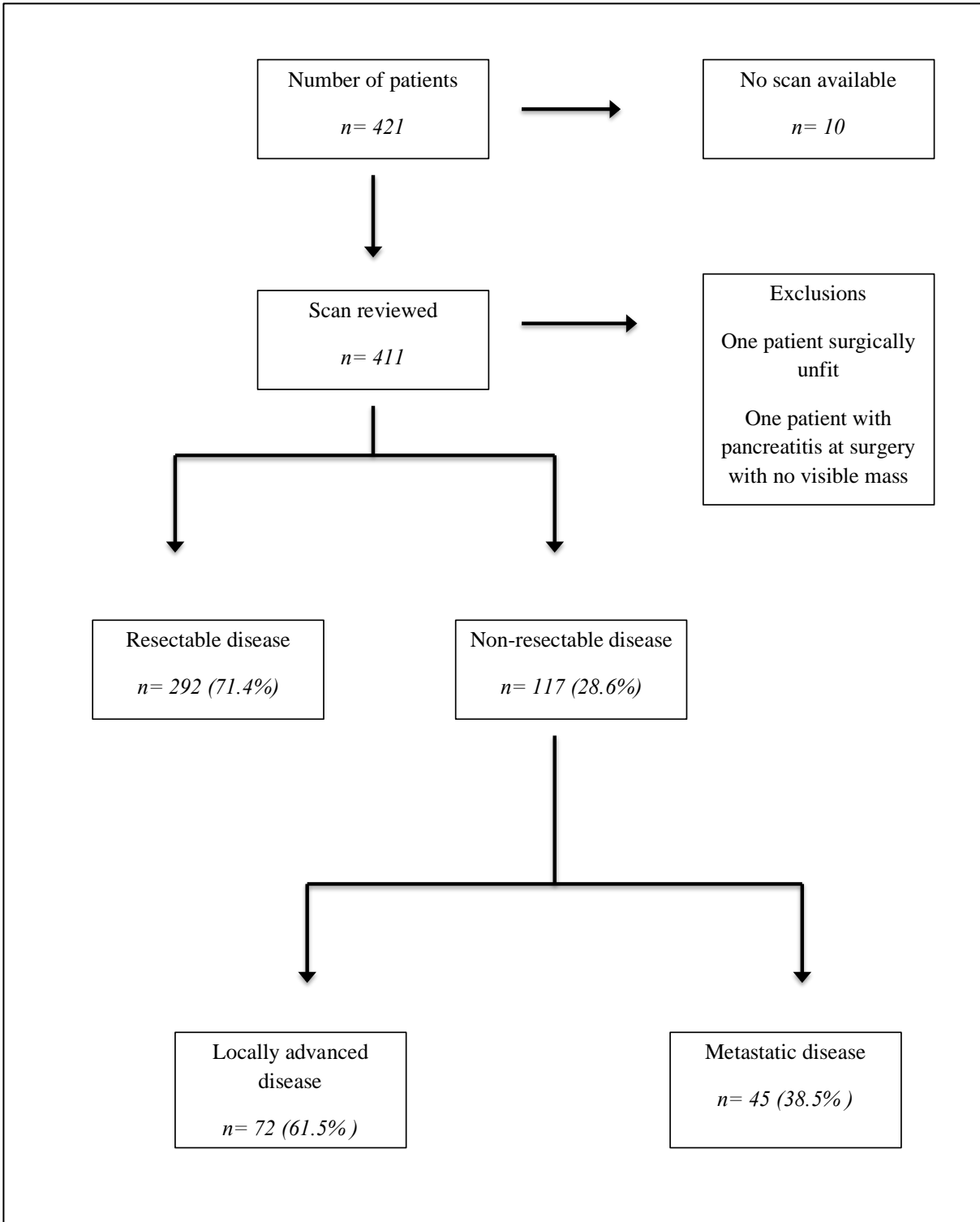
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394 Figure 2. Flow chart of patients undergoing surgery for PC between January 2006 and  
 395 January 2014

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| <i>n</i> = 409                  |         | Monophasic<br>(134, 32.7%) | Biphasic<br>(149, 36.4%) | Triphasic<br>(126, 31%) | P      |
|---------------------------------|---------|----------------------------|--------------------------|-------------------------|--------|
| Hospital                        | A (119) | 20 (16.8)                  | 52 (43.7)                | 46 (38.6)               | 0.0001 |
|                                 | B (97)  | 45 (46.4)                  | 50 (51.5)                | 2 (2.1)                 |        |
|                                 | C (78)  | 24 (30.7)                  | 9 (11.5)                 | 45 (57.7)               |        |
|                                 | D (71)  | 24 (33.8)                  | 21(29.5)                 | 26 (36.6)               |        |
|                                 | E (44)  | 21 (47.7)                  | 17 (38.6)                | 6 (13.6)                |        |
| AI (16)                         |         | 3 (2.4)                    | 8 (5.4)                  | 5 (4)                   | 0.398  |
| VI (47)                         |         | 20 (15)                    | 11 (7.4)                 | 16 (12.7)               | 0.122  |
| RL (101)                        |         | 28 (21)                    | 42 (28.2)                | 31 (24.6)               | 0.83   |
| Tumour visible (250)            |         | 72 (53.7)                  | 99 (66.4)                | 79 (62.7)               | 0.83   |
| Median tumour size<br>(average) |         | 25.25<br>(11.5-70)         | 26.25<br>(10.5-58)       | 27.75<br>(8-64.5)       | 0.39   |
| Resection completed<br>(292)    |         | 102 (76.1)                 | 107 (71.8)               | 83 (65.8)               | 0.187  |

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398 Table 1. Radiological findings and surgical resection rate according to the number of CT scan  
399 phases for 409 patients undergoing attempted surgical resection for PC

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| Tumour origin                                   | N (%)      | Median tumour size<br>(range) mm | Histological lymph<br>node involvement<br>(%) |
|---|------------|----------------------------------|---|
| Pancreatic adenocarcinoma                       | 132 (45.2) | 30 (12-65)                       | 122 (92.4)                                    |
| Ampullary adenocarcinoma                        | 66 (22.6)  | 25 (5-80)                        | 37 (56)                                       |
| Bile duct adenocarcinoma                        | 47 (16.1)  | 25 (10-70)                       | 25 (53.2)                                     |
| Duodenal adenocarcinoma                         | 7 (2.4)    | 40 (30-55)                       | 4 (47)  |
| Tubulo-villous adenoma                          | 15 (5.1)   | 30 (24-55)                       |   |
| Inflammatory disease                            | 12 (4.1)   |                                  |   |
| Neuroendocrine tumour                           | 6 (2)      | 18 (10-25)                       | 3 (50)  |
| Metastasis                                      | 4 (1.4)    | 35 (25-45)                       |   |
| Gastro Intestinal Stromal cell<br>tumour (GIST) | 1 (0.03)   |                                  | 0 (0)   |
| Others (Benign)                                 | 2 (0.6)    |                                  |   |

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410 Table 2. Histological outcome of 292 patients undergoing surgical resection for presumed  
411 PC.

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| Imaging characteristic         | Tumour resectability |                   | UVA   | MVA      |                       |       |
|--------------------------------|----------------------|-------------------|-------|----------|-----------------------|-------|
|                                | Yes<br>(292)         | No<br>(117)       | p     | Exponent | 95% CI of<br>Exponent | p     |
| Median tumour size (mm)(range) | 25.5<br>(8-70)       | 28<br>(11.5-64.5) | 0.01  | 0.46     | (0.193-1.084)         | 0.076 |
| RL (101)<br>(%)                | 63<br>(21.6)         | 39<br>(32.8)      | 0.017 | 0.51     | (0.272-0.949)         | 0.047 |
| AI (16)<br>(%)                 | 2<br>(0.68)          | 14<br>(11.7)      | 0.000 | 0.05     | (0.007-0.445)         | 0.007 |
| VI (47)<br>(%)                 | 17<br>(5.82)         | 30<br>(25.2)      | 0.000 | 0.31     | (0.152-0.638)         | 0.001 |

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421 Table 3. Univariate and multivariate analysis of the association of the preoperative  
422 radiological risk factors and surgical resectability of PC in 409 patients

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| <i>n</i> =117                                   | Local progression    | Metastatic disease   | Chi Sq | P     |
|---|----------------------|----------------------|--------|-------|
| Radiological finding                            | ( <i>n</i> = 72)     | ( <i>n</i> = 45)     |        |       |
| Tumour visible (84, 71.8%)                      | 49<br>(58.3)         | 35<br>(41.6)         | 1.3    | 0.256 |
| Median tumour size (mm)<br>(range)              | 28.25<br>(11.5-64.5) | 27.75<br>(16.5-55.5) | 0.838  | 0.36  |
| RL (38, 32.5%)                                  | 23 (60.5)            | 15 (39.5)            | 0.024  | 0.876 |
| AI (16, 13.7%)                                  | 9 (56.2)             | 5 (31.25)            | 0.051  | 0.822 |
| VI (30, 25.6%)                                  | 22 (73.3)            | 8 (26.6)             | 2.37   | 0.123 |
| No adverse radiological findings<br>(54, 46.1%) | 32 (59.2)            | 22 (40.7)            | 0.22   | 0.639 |

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436 Table 4. Reasons for non-resection (local invasion or metastatic disease) among 117 patients  
 437 undergoing attempted surgical resection for PC with different pre-operative radiological  
 438 findings

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