Cancer Imaging (2011) **11,** 116–122
DOI: 10.1102/1470-7330.2011.0019

ORIGINAL ARTICLE

MDCT evaluation of the growth kinetics of serous and benign mucinous cystic neoplasms of the pancreas

Hamid Chalian[a], Hüseyin G. Töre[a], Pedram Rezai[a], David J. Bentrem[b] and Vahid Yaghmai[a]

[a]Department of Radiology, Northwestern Memorial Hospital, Northwestern University-Feinberg School of Medicine, Chicago, IL, USA; [b]Department of Surgery, Northwestern Memorial Hospital, Northwestern University-Feinberg School of Medicine, Chicago, IL, USA

Corresponding address: Vahid Yaghmai, MD, Associate Professor and Medical Director of CT Imaging, Department of Radiology, Northwestern Memorial Hospital, Northwestern University-Feinberg School of Medicine, 676 North Saint Clair Street Suite 800, Chicago, IL 60611, USA.
Email: v-yaghmai@northwestern.edu

Date accepted for publication 13 June 2011

Abstract

We assessed the growth kinetics of pathologically proven benign neoplastic cystic lesions of the pancreas. The volume and longest axial diameter (LAD) of 20 pathologically proven pancreatic cystic lesions (12 mucinous cystic neoplasms (MCN) and 8 serous cystadenomas (SCN)) on 2 multidetector computed tomography scans, obtained before resection, were measured. Reciprocal of doubling time, doubling time and growth rate based on volume and LAD were calculated. A P value <0.05 was considered significant. For all cysts, growth kinetics based on volume were: reciprocal of doubling time (mean = 3.03, median=1.0), doubling time (mean = 644, median = 388 days) and growth rate (mean = 74.7, median = 5.7 ml/year). Results based on LAD were: reciprocal of doubling time (mean = 3.09, median = 1.3), doubling time (mean = 752, median = 273 days) and growth rate (mean = 24.5, median = 5.6 mm/year). These variables were not statistically different between MCNs and SCNs ($P > 0.05$ in all instances). Reciprocal of doubling time based on volume and LAD were comparable ($P > 0.05$). We concluded that the mean reciprocal of doubling time was 3.03 and 3.09 using volume and LAD, respectively. This may aid in designing follow-up guidelines for pancreatic cysts.

Keywords: *Pancreas; cystic neoplasm; benign; doubling time; growth rate.*

Introduction

Due to the improvements in imaging technologies in the modern era, pancreatic cystic lesions are identified much more frequently as an incidental finding[1,2]. Although most pancreatic cysts have an inflammatory nature, differential diagnosis and management of neoplastic cystic lesions of pancreas are still a clinical challenge. Neoplastic cystic lesions of the pancreas have different histologic types with serous cystadenomas (SCNs), mucinous cystic neoplasms (MCNs) and intraductal papillary mucinous neoplasms (IPMNs) making up more than 90%[3]. Pathologically, neoplastic cystic lesions of the pancreas may be completely benign, a precursor of malignancy or may already harbor malignancy[4]. This wide range of malignant potential makes imaging follow-up a good option for some neoplastic cystic lesions of the pancreas[5,6].

There is no uniform consensus for imaging follow-up of pancreatic cysts. Several reports suggest noninvasive follow-up of asymptomatic cysts less than 3 cm in size[6–8]. As there is a lack of information on the natural history and growth kinetics of these lesions, different follow-up strategies have been suggested for neoplastic cystic lesions of the pancreas[6,7]. To our knowledge there is no report in the literature of the growth kinetics of MCNs. The growth kinetics of pancreatic cysts are commonly based on a single dimensional measurement

This paper is available online at http://www.cancerimaging.org. In the event of a change in the URL address, please use the DOI provided to locate the paper.

or the extrapolated volume of the cysts[9,10]. We have shown previously that extrapolated volume may overestimate the true volume of pancreatic cysts[11]. We aimed to assess the growth kinetics of benign pancreatic cystic lesions based on both the true volume and the longest axial diameter (LAD) of the cysts, which may be useful for designing a more objective guideline for the follow-up of pancreatic cysts.

Materials and methods

This retrospective Health Insurance Portability and Accountability Act (HIPAA) compliant study was approved by our institutional review board. Patient informed consent was waived. Patient selection was performed in our departmental electronic radiology report database search engine using the following key words: "pancreatic cyst" and "MDCT." A total of 119 (97 benign, 22 premalignant/malignant) pathologically proven pancreatic cysts that underwent multidetector computed tomography (MDCT) before resection were included. Ninety-nine patients (including all 22 premalignant/malignant cysts) had one CT available before resection and, therefore, could not be evaluated for growth kinetics. Reason for having one CT in these 99 patients included suspicious morphology and size of the lesion that warranted immediate resection, follow-up with magnetic resonance imaging (MRI) or lack of availability of the baseline CT that was obtained at an outside institution. Our study population, therefore, consisted of 20 patients with surgically proven benign cysts who had 2 MDCT examinations before resection, allowing calculation of growth kinetics.

MDCT imaging protocol

All MDCT scans were obtained using a Siemens Somatom Sensation 16- or 64-slice scanner (Siemens Medical Solutions) or GE LightSpeed 4-slice scanner (GE HealthCare). Image acquisition consisted of a triphasic pancreatic protocol that included unenhanced images of the abdomen, followed by pancreatic parenchymal phase of the abdomen obtained at 40 s and portal venous phase of the abdomen and pelvis obtained at 70 s. The pancreatic parenchymal phase was obtained using a 0.6-, 0.75- or 1.25-mm collimation and 2- or 2.5-mm slice thickness during intravenous administration of 125 ml of iohexol-350 (GE Healthcare; total dose of iodine, 43.75 g) at the rate of 4 ml/s. Intravenous contrast was administered via an antecubital vein using an 18- to 20-gauge intravenous catheter and a mechanical injector (Stellant, Medrad).

Image Analysis

Image analysis was done by single reader using the pancreatic parenchymal phase images. Commercially available volumetry software (CT Oncology; Siemens Medical Solutions) was used on an image-processing workstation (Leonardo Workstation, Syngo 2008 A VE26A Multi-Modality platform; Siemens Medical Solutions) for segmentation of the cysts and volume analysis. The application of this software in the segmentation of abdominal masses has been described previously by Keil et al.[12]. The graphic user interface is divided into 4 small screens: axial, coronal, sagittal and three-dimensional views. The software segments the entire lesion automatically and generates a volume of interest (VOI) around the line drawn across the cyst in one image plane by the investigator. This stage is followed by three-dimensional reasoning to remove adjacent normal pancreatic tissue. The included regions are indicated by a colored edge. This process was done for both baseline and follow-up MDCT images side by side for better comparison and fine-tuning of the segmentation. After finalizing the segmentation, the software analyzed the segmented regions and provided pancreatic cyst volume and LAD (Fig. 1). Image analysis time for volumetry of the lesions was measured. High interobserver reproducibility of this software has been previously reported[11].

Doubling time, reciprocal of doubling time and growth rate calculation

The volume doubling time was calculated by using the Schwartz formula[13]: volume doubling time $= (t_2 - t_1) \times \log_2 / (\log V_2 - \log V_1)$ where V_1 is the segmented volume in the base line study, V_2 is the segmented volume in the follow-up study and $t_2 - t_1$ is the time interval between studies. Since the doubling time is an exponential function, its calculation may not provide normally distributed numbers. This limitation has been addressed in the literature by converting doubling time to the reciprocal of doubling time (reciprocal of doubling time $= 365$/doubling time) to obtain a linear function[14–17]. Reciprocal of doubling time is the linear representation of tumor growth rate. When there is no change in size, reciprocal of doubling time approaches 0 and a negative and positive reciprocal of doubling time corresponds to lesion shrinkage and expansion, respectively, from baseline to follow-up examination. We also calculated the growth rate to make it possible to compare for our results with previously published studies on growth kinetics of pancreatic cystic lesions. Volume growth rate was calculated using the following equation: volume growth rate $= (V_2 - V_1)/(t_2 - t_1)$. For calculation of the doubling time, the reciprocal of doubling time and the growth rate with reference to LAD, the same equations were used by substituting LAD for volume[17]. Doubling time is inversely proportional to reciprocal of doubling time and growth rate[16,18].

Statistical analysis

We used MedCalc for Windows, version 9.6.4.0 (MedCalc Software, Mariakerke, Belgium) for statistical

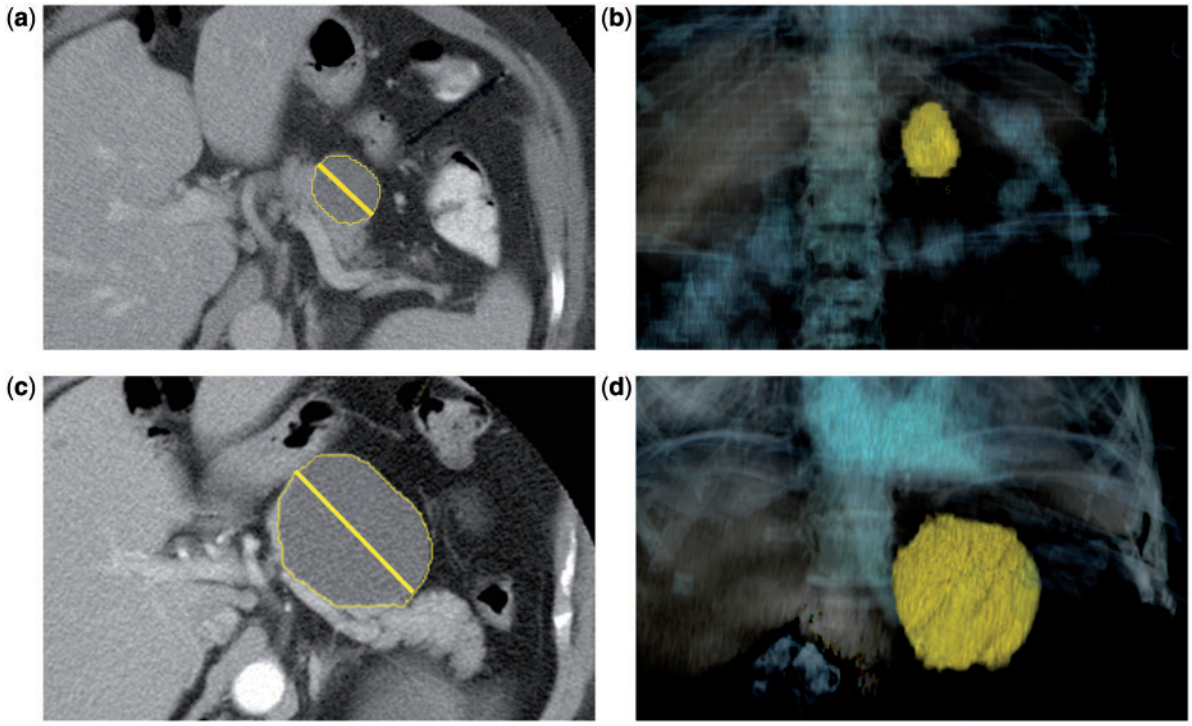

Figure 1 **MDCT images of a pancreatic MCN in a 67-year-old woman. (a) Baseline axial and (b) volume rendered images. The LAD (3.34 cm) and segmented volume (16.9 ml) of the cyst were calculated. (c) Axial and (d) volume rendering MDCT images 251 days later. LAD and segmented volume have increased to 8.13 cm and 184 ml, respectively.**

analysis. Mean or median (95% confidence interval (CI)) values for segmented volume, LAD, doubling time, growth rate and reciprocal of doubling time were calculated. Chi-square test was used for assessment of the relationship between gender and cyst type. Wilcoxon test and paired-sample *t*-test were used for identifying the change in tumor size between 2 observations and comparing the reciprocal of doubling time between different methods (volume vs LAD). The Mann–Whitney test and Student's *t*-test were used for comparing the variables between MCNs and SCNs. The significance level was set at 0.05.

Results

Demographics

The study population consisted of 20 pathologically proven pancreatic cystic lesions (12 MCNs and 8 SCNs) with at least 2 MDCT scans performed before resection during the period between October 2005 and October 2007. Seven cysts were resected after their diameter increased to more than 3 cm. Others were resected because they were symptomatic or at the patient's request. No cyst was stable in size during the follow-up period. Five (25%) cysts were located in the head, 6 (30%) were located in the body and 9 (45%) were located in the tail of the pancreas. There were 14 (70%) female and 6 (30%) male patients. The mean age of the females was 60 ± 15 years (range 20–77 years) and 47 ± 17 years (range 33–70 years) for males ($P = 0.09$). Age was also comparable between MCNs (61 ± 15 years) and SCNs (49 ± 16 years, $P = 0.08$). MCNs were more prevalent ($P = 0.019$) in females (11/12, 92%) and SCNs were more common in males (5/8, 63%). The median time interval between obtaining MDCT scans was 226 days (range 35–1454 days, 95% CI 106–364 days).

MDCT volumetry

Median cyst volume in the baseline study was 2.25 ml (range 0.35–170 ml, 95% CI 1.07–4.4 ml). Median volume for the follow-up study was 6.7 ml (range 0.63–187 ml, 95% CI 1.8–28.7 ml). Median LAD was 1.9 cm (range 0.94–8.3 cm, 95% CI 1.3–2.6 cm) at baseline and 2.4 cm (range 0.98–8.6 cm, 95% CI 1.6–4.6 cm) at follow-up (Table 1). The mean time required for volumetry of the lesions was 27 ± 9 s (range 19–45 s).

Mean values for the reciprocal of doubling time with reference to volume were 3.03 (95% CI 0.64–5.4) in the whole cohort, 3.6 (95% CI −0.46 to 7.7) in MCNs and 2.1 (95% CI 0.59–3.6) in SCNs. The reciprocal of doubling time based on volume and LAD was comparable between MCNs and SCNs ($P > 0.05$). The reciprocal of doubling time was also comparable between different

methods of measurement (volume vs LAD) in the whole cohort, MCNs and SCNs ($P > 0.05$ in all instances) (Fig. 2). The mean and median values for the reciprocal of doubling time, doubling time and growth rate with reference to segmented volume and LAD are presented in Table 2. All variables were comparable between MCNs and SCNs ($P > 0.05$ in all instances) (Figs. 3 and 4 and Table 2).

Table 1 Volumetry and LAD of serous and benign mucinous pancreatic cystic neoplasms on baseline and follow-up measurements

	Baseline volume	Follow-up volume	*P* value
Volume (ml)			
MCN			<0.001
Median	3.1	6.7	
95% CI	1–4.4	2.2–62.8	
Range	0.35–16.9	0.89–184	
SCN			<0.05
Median	1.8	8.4	
95% CI	0.53–130	0.65–140	
Range	0.47–170	0.63–187	
Total			<0.001
Median	2.25	6.9	
95% CI	1.07–4.4	1.8–28.7	
Range	0.35–170	0.63–187	
LAD (cm)			
MCN			<0.05
Median	2.0	2.4	
95% CI	1.3–2.8	1.7–4.7	
Range	1.0–3.3	1.3–8.6	
SCN			>0.05
Median	1.6	2.6	
95% CI	1.07–6.8	1–7.2	
Range	0.94–8.3	0.98–8.6	
Total			<0.05
Median	1.9	2.4	
95% CI	1.32–2.6	1.6–4.6	
Range	0.94–8.3	0.98–8.6	

P values indicate differences between baseline and follow-up measurements of the entire cohort, MCNs and SCNs.

Discussion

Pancreatic cystic lesions are more common than previously recognized and are being increasingly identified as an incidental finding due to the advances in imaging

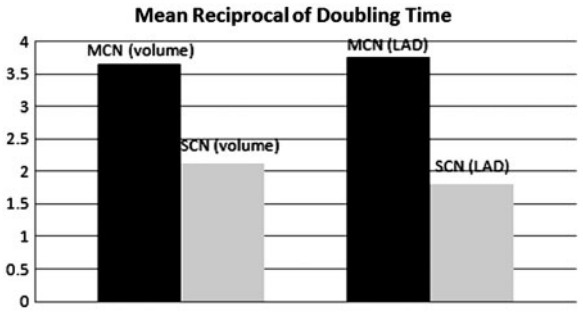

Figure 2 **Mean reciprocal of doubling time calculated for MCNs, 3.6 (95% CI −0.46 to 7.7) and SCNs, 2.1 (95% CI 0.59–3.6) based on volume. Reciprocal of doubling time was also measured for MCNs, 3.7 (95% CI −0.24 to 7.7) and SCNs, 1.8 (95% CI −0.1 to 3.8) based on LAD. Reciprocal of doubling time was not statistically different ($P > 0.05$) between different pathologies as well as different methods of measurement (volume vs LAD).**

Table 2 Reciprocal of doubling time, growth rate and doubling time measurements of serous and benign mucinous pancreatic cystic neoplasms

	Total	MCN	SCN	*P* value
Reciprocal of doubling time				
Volume				
Mean (95% CI)	3.03 (0.64–5.4)	3.6 (−0.46 to 7.7)	2.1 (0.59–3.6)	0.52
Median (95% CI)	1.0 (0.6–3.4)	0.7 (0.54–4.5)	1.6 (0.17–4.3)	
LAD				
Mean (95% CI)	3.09 (0.57–5.6)	3.7 (−0.24 to 7.7)	1.8 (−0.1 to 3.8)	0.47
Median (95% CI)	1.3 (0.46–2.3)	0.8 (0.4–6.3)	1.5 (0.29–4.8)	
Doubling time (day)				
Volume				
Mean (95% CI)	644 (275–1014)	620 (137–1103)	649 (−110 to 1408)	0.93
Median (95% CI)	388 (107–608)	518 (85–674)	137 (73–2093)	
LAD				
Mean (95% CI)	752 (195–1309)	885 (27–1742)	509 (−147 to 1164)	0.51
Median (95% CI)	273 (158–786)	439 (60–1059)	244 (90–1511)	
Growth rate				
Volume (ml/year)				
Mean (95% CI)	74.7 (−4.5 to 154)	117.2 (−16 to 251)	11.2 (−1.8 to 24.1)	0.19
Median (95% CI)	5.7 (0.7–28.3)	10 (2–213)	3.6 (1.3–28)	
LAD (mm/year)				
Mean (95% CI)	24.5 (3.54–45.6)	31.6 (−1.6 to 64.6)	11.7 (0.83–24.2)	0.61
Median (95% CI)	5.6 (2.5–13.6)	5.6 (2–7.9)	7 (3.8–30.5)	

P values indicate differences between MCNs and SCNs.

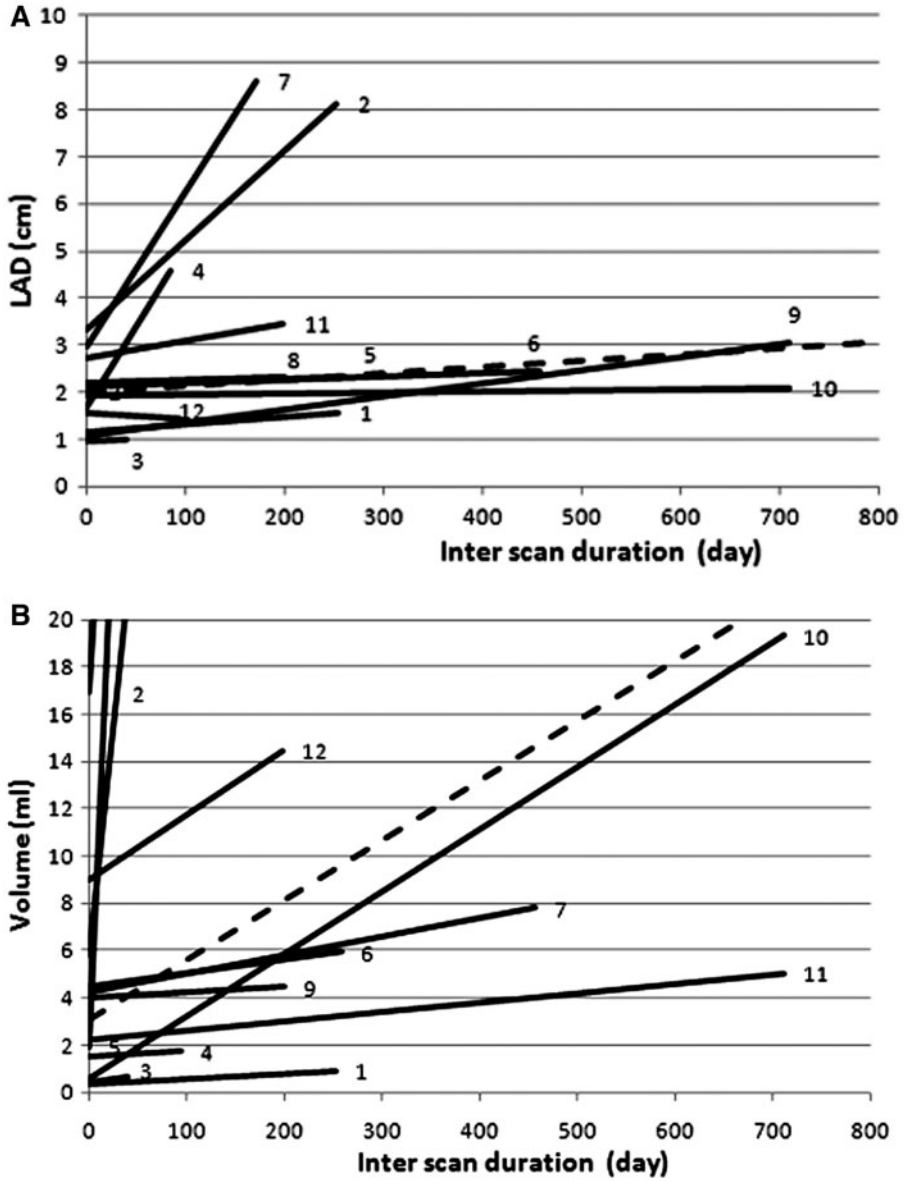

Figure 3 **Growth over time in MCNs. (a) Median growth rate based on LAD = 5.6 mm/year (95% CI 2–7.9). (b) Median growth rate based on volume = 10 ml/year (95% CI 2–213).**

modalities, particularly in the last decade[1,2,19]. Cystic pancreatic neoplasms have different histological types with SCN, MCN and IPMN accounting for 90% of primary cystic neoplasms of the pancreas[3]. Among the true cystic neoplasms of the pancreas, SCNs are the most prevalent followed by MCNs and IPMNs[20]. Based on the World Health Organization (WHO) histological classification for tumors, 3 grades have been described for cystic neoplasms of the pancreas: benign, low-grade malignant (borderline), and malignant (carcinoma in situ and invasive cancer)[4]. Detection of a pancreatic cyst prompts concerns with regard to the best management strategy. Substantial limitations exist in definitive identification of the malignant potential of the pancreatic cystic neoplasms despite the many improvements in imaging techniques. Therefore, management of these cystic lesions remains a clinical dilemma. Although it is clear that a malignant lesion should be surgically resected after considering the patient's surgical risk, there is no evidence-based strategy for the best follow-up plan for non-resected pancreatic cystic lesions. Different follow-up intervals have been proposed in the literature. Some have suggested annual imaging surveillance for SCNs less than 4 cm[6]. Others have recommended the following strategy for non-resected MCNs and IPMNs: annual imaging if the lesion is less than 10 mm in size, 6–12 monthly follow-up for lesions between 10 and 20 mm, and 3–6 monthly follow-up for lesions larger than 20 mm[7]. We believe that better understanding of the growth kinetics of pancreatic

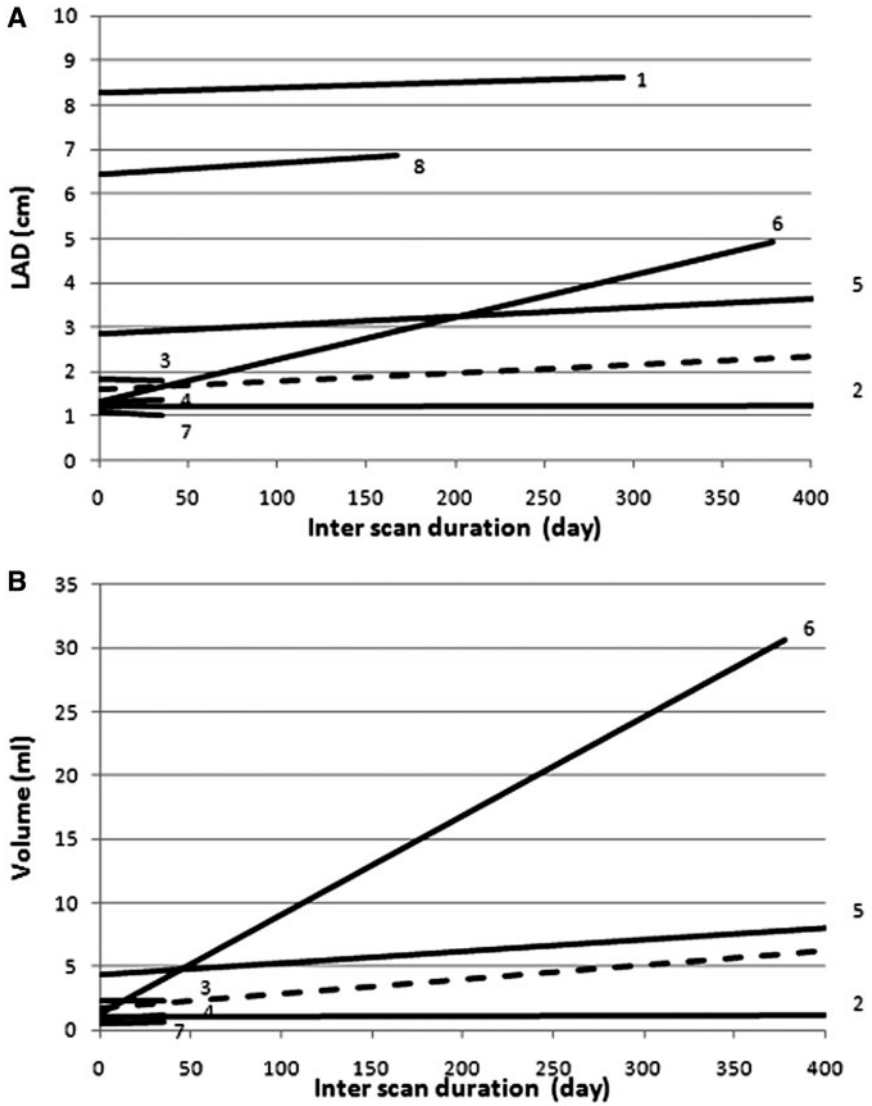

Figure 4 **Growth over time in SCNs. (a) Median growth rate based on LAD = 7 mm/year (95% CI 3.8–30.5). (b) Median growth rate based on volume = 3.6 ml/year (95% CI 1.3–28). Values for cases 1 and 8 were out of the scales of (b).**

cystic neoplasms can help with designing a more evidence-based follow-up strategy for these lesions.

With the evolving imaging technology that allows acquisition of high-resolution volumetric images, volumetric analysis of pancreatic cysts has become possible[11,12,21]. We analyzed the growth kinetics of MCNs and SCNs of the pancreas based on their volume and LAD. Volumetric evaluation of the growth rate has the advantage of considering the entire tumor size instead of using the longest diameter as a surrogate for the tumor volume. Volumetric growth rate of benign pancreatic cystic masses has not been previously reported. In our analysis, the mean reciprocal of doubling time based on volume was 3.03, 3.6 and 2.1 for the whole cohort, MCNs and SCNs, respectively. The mean reciprocal of doubling time based on LAD was calculated as 3.09, 3.7 and 1.8 for the whole cohort, MCNs and SCNs, respectively. In our analysis there was no difference between the reciprocal of doubling time measured based on volume and LAD. This might be secondary to the limited power due to the relatively small sample size in our analysis.

The growth rate calculated based on volume was 10 ml/year and 3.6 ml/year for MCNs and SCNs, respectively. In order to be able to compare our data with previous reports that have used LAD, we also calculated growth variables based on LAD. Our results demonstrated that the growth rate was 5.6 mm/year for MCNs and 7 mm/year for SCNs when using LAD (Figs. 3a and 4a). Of interest, a few of these lesions showed very fast growth rates despite being benign. In a study performed on 24 SCNs, Tseng et al.[9] reported a comparable growth rate of 6 mm/year for SCNs. Similar parameters for benign MCNs have not been reported and, therefore, we were unable to compare our results with other reports.

In our analysis, the median doubling time for benign MCNs and SCNs was 439 days and 244 days based on

LAD and 518 days and 137 days based on volume, respectively. Tseng et al.[9] reported a doubling time of 2.84 years (1036 days) for SCNs larger than 4 cm and doubling time of 0.64 years (233 days) for SCNs smaller than 4 cm based on volume. The difference between our data and Tseng et al.'s data is most likely due to the method of calculating volumetric doubling time. Tseng et al. used extrapolated volume from their data, whereas we used the true volume that was segmented on high-resolution CT scans. We have shown previously that extrapolated volume may overestimate the true volume. According to our previous report, volume measurements based on LAD might have up to 50% overestimation compared with the true volume measured by MDCT-based segmentation[11].

This study has some limitations. First, our relatively small sample size may limit the power of analysis in finding a statistically significant difference between the growth kinetics of SCNs and MCNs. However, due to strict inclusion criteria for this type of study, large samples may be difficult to obtain. Second, we did not find benign IPMNs with serial MDCT images in our database to provide a more comprehensive depiction of the growth kinetics of benign neoplastic cysts of the pancreas. Third, growth kinetics of benign and malignant pancreatic cystic lesions might be different and hypothetically can help in the identification of malignant potential of these lesions. Further investigations including malignant neoplastic cysts of the pancreas are warranted to develop an algorithm for follow-up of cystic pancreatic neoplasms.

In conclusion, our findings show similar growth rates for SCNs and benign MCNs of the pancreas. This information may be helpful in developing an algorithm for follow-up imaging of pancreatic cystic lesions.

Acknowledgments

Hamid Chalian, MD, Hüseyin Gürkan Töre, MD and Pedram Rezai, MD were supported by educational grants from Siemens Healthcare. Northwestern University has a Master Research Agreement with Siemens Healthcare.

References

[1] Fernandez-del Castillo C, Targarona J, Thayer SP, Rattner DW, Brugge WR, Warshaw AL. Incidental pancreatic cysts: clinicopathologic characteristics and comparison with symptomatic patients. Arch Surg 2003; 138: 427–3. discussion 33–4.

[2] Sahani D, Prasad S, Saini S, Mueller P. Cystic pancreatic neoplasms evaluation by CT and magnetic resonance cholangiopancreatography. Gastrointest Endosc Clin North Am 2002; 12: 657–72. doi:10.1016/S1052-5157(02)00022-3.

[3] Fernandez-del Castillo C, Warshaw AL. Cystic tumors of the pancreas. Surg Clin North Am 1995; 75: 1001–16.

[4] Klöppel G, Solcia E, Longnecker DS, Capella C, Sobin L. Histological typing of tumours of the exocrine pancreas. World Health Organization international histological classification of tumours. 2nd ed. New York: Springer-Verlag; 1998.

[5] Sahani DV, Kadavigere R, Saokar A, Fernandez-del Castillo C, Brugge WR, Hahn PF. Cystic pancreatic lesions: a simple imaging-based classification system for guiding management. Radiographics 2005; 25: 1471–84. doi:10.1148/rg.256045161.

[6] Sahani DV, Miller JC, del Castillo CF, Brugge WR, Thrall JH, Lee SI. Cystic pancreatic lesions: classification and management. J Am Coll Radiol 2009; 6: 376–80. doi:10.1016/j.jacr.2008.10.004.

[7] Tanaka M, Chari S, Adsay V, *et al.* International consensus guidelines for management of intraductal papillary mucinous neoplasms and mucinous cystic neoplasms of the pancreas. Pancreatology 2006; 6: 17–32. doi:10.1159/000090023.

[8] Allen PJ, D'Angelica M, Gonen M, *et al.* A selective approach to the resection of cystic lesions of the pancreas: results from 539 consecutive patients. Ann Surg 2006; 244: 572–82.

[9] Tseng JF, Warshaw AL, Sahani DV, Lauwers GY, Rattner DW, Fernandez-del Castillo C. Serous cystadenoma of the pancreas: tumor growth rates and recommendations for treatment. Ann Surg 2005; 242: 413–19. discussion 9–21.

[10] Kang MJ, Jang JY, Kim SJ, *et al.* Cyst growth rate predicts malignancy in patients with branch duct intraductal papillary mucinous neoplasms. Clin Gastroenterol Hepatol 2011; 9: 87–93. doi:10.1016/j.cgh.2010.09.008.

[11] Aghaei Lasboo A, Rezai P, Yaghmai V. Morphological analysis of pancreatic cystic masses. Acad Radiol 2010; 17: 348–51. doi:10.1016/j.acra.2009.09.013.

[12] Keil S, Behrendt FF, Stanzel S, *et al.* Semi-automated measurement of hyperdense, hypodense and heterogeneous hepatic metastasis on standard MDCT slices. Comparison of semi-automated and manual measurement of RECIST and WHO criteria. Eur Radiol 2008; 18: 2456–65. doi:10.1007/s00330-008-1050-6.

[13] Schwartz M. A biomathematical approach to clinical tumor growth. Cancer 1961; 14: 1272–94. doi:10.1002/1097-0142(196111/12)14:6<1272::AID-CNCR2820140618>3.0.CO;2-H.

[14] Jennings SG, Winer-Muram HT, Tann M, Ying J, Dowdeswell I. Distribution of stage I lung cancer growth rates determined with serial volumetric CT measurements. Radiology 2006; 241: 554–63. doi:10.1148/radiol.2412051185.

[15] Honda O, Johkoh T, Sekiguchi J, *et al.* Doubling time of lung cancer determined using three-dimensional volumetric software: comparison of squamous cell carcinoma and adenocarcinoma. Lung Cancer 2009; 66: 211–17. doi:10.1016/j.lungcan.2009.01.018.

[16] Mehrara E, Forssell-Aronsson E, Ahlman H, Bernhardt P. Specific growth rate versus doubling time for quantitative characterization of tumor growth rate. Cancer Res 2007; 67: 3970–5. doi:10.1158/0008-5472.CAN-06-3822.

[17] Zhang J, Kang SK, Wang L, Touijer A, Hricak H. Distribution of renal tumor growth rates determined by using serial volumetric CT measurements. Radiology 2009; 250: 137–44. doi:10.1148/radiol.2501071712.

[18] Mehrara E, Forssell-Aronsson E, Ahlman H, Bernhardt P. Quantitative analysis of tumor growth rate and changes in tumor marker level: specific growth rate versus doubling time. Acta Oncol 2009; 48: 591–7. doi:10.1080/02841860802616736.

[19] Kimura W, Nagai H, Kuroda A, Muto T, Esaki Y. Analysis of small cystic lesions of the pancreas. Int J Pancreatol 1995; 18: 197–206.

[20] Brugge WR, Lauwers GY, Sahani D, Fernandez-del Castillo C, Warshaw AL. Cystic neoplasms of the pancreas. N Engl J Med 2004; 351: 1218–26. doi:10.1056/NEJMra031623.

[21] Rezai P, Mulcahy MF, Tochetto SM, Berggruen S, Yaghmai V. Morphological analysis of pancreatic adenocarcinoma on multidetector row computed tomography: implications for treatment response evaluation. Pancreas 2009; 38: 799–803. doi:10.1097/MPA.0b013e3181ac7511.