Intraductal papillary mucinous neoplasm’s 100 most significant manuscripts: A bibliometric analysis

Daniel Hughes, Ioan Hughes, Arfon GMT Powell, Bilal Al-Sarireh

ABSTRACT

Aims: The aim of this bibliometric analysis was to identify the main topics and publications that have enhanced our understanding and influenced the management of intraductal papillary mucinous neoplasm (IPMN). Methods: The Thompson Reuters Web of Science database was searched using the terms ‘Intraductal papillary mucinous neoplasm’, or ‘IPMN’ to identify all English language manuscripts for the study. The 100 most cited articles were further analyzed by journal, topic, year, author and institution. Results: Total 2,833 eligible manuscripts were identified. The median (range) citation number was 129 (93–1006). The most cited paper presented consensus guidelines regarding the management of IPMN (1006 citations). The Annals of Surgery published the highest number of manuscripts (n = 13) and subsequently had the highest number of citations (n = 2889). The USA published most manuscripts within the top 100 (n = 46). The most discussed topic was IPMN management (n = 29), incorporating diagnosis and surgery. The second most commonly discussed topic was histology (n = 18). Conclusion: This bibliometric analysis highlights how advances in the histological evaluation of IPMN have influenced current management strategies for IPMN. This manuscript highlights the most cited and influential references related to IPMN and serves as a guide to the most popular IPMN research themes.

Keywords: Bibliometric analysis, Intraductal papillary mucinous neoplasm

INTRODUCTION

Intraductal papillary mucinous neoplasms (IPMN) are pancreatic tumors that arise from the pancreatic ductal system [1]. Histological analyses of these tumors reveal mucin secreting columnar epithelium with a variable degree of dysplastic epithelium [2]. Current evidence suggests that these cystic tumors have the potential to undergo malignant transformation as part of the dysplasia-carcinoma sequence, with 30–50% tumors undergoing such transformation [2, 3]. For this reason, research has been focussed on expanding our knowledge...
regarding the molecular aspects, clinical presentation and management of these pancreatic cystic tumors. Advances in our knowledge of IPMN will influence and subsequently transform clinical practice enabling the creation of suitable treatment strategies and surveillance protocols.

A citation rank list enables identification of published research that bears most intellectual influence [4]. Once a publication is referenced by another peer-reviewed article, a citation is received. It is likely that original research with the most influence over the scientific community would be cited several times. The process of citation analysis consists of ranking articles based on the number of citations it has received. This technique can also be utilized to rank journals based on their impact on the scientific community [4].

To date several medical specialities have conducted a citation rank analysis in order to highlight the most influential papers within their own field. This includes general surgery, plastic surgery and trauma and orthopaedic surgery [4–6]. Currently, no study has assessed for the most influential IPMN manuscripts. An examination of this data would allow an understanding of how our knowledge regarding IPMN has changed and how this has impacted on clinical management. The aim of this study was to identify the studies of greatest clinical influence that has enhanced our knowledge regarding IPMN.

MATERIALS AND METHODS

The Thomson Reuters Web of Science citation indexing database was searched. The following search terminology was utilized, the term “Intraductal papillary mucinous neoplasm” or “IPMN” and “panc*” was used. The Web of Science database search was completed by two independent researchers in order to ensure that appropriate studies were included. A method described by Paladugu et al. was applied in order to review the data. The returned search from the Thomson Reuters Web of Science database was filtered to contain full manuscripts of English language only, which were subsequently sorted by number of citations [7]. Exclusion criteria consisted of non-English articles and articles that did not focus on IPMN related research. The 100 most cited manuscripts were noted. Data was extracted from each manuscript for title, author list, topic, country of origin and year of publication. The individual, and five year impact factor of each included journal was noted.

RESULTS

The Thomson Reuters Web of Science database search produced 2,833 full-length, English language papers. Table 1 highlights the 100 most cited IPMN articles [8-106]. The total number of citations ranged from 1006 by Tanaka et al. (International consensus on the management of intraductal papillary mucinous neoplasm of the pancreas) [8] to 93 by Bernard et al. (Intraductal papillary mucinous tumors of the pancreas: predictive criteria of malignancy according to the pathological examination of 53 cases) [106]. The most recent published manuscript was produced by Kallen et al. in 2016 (Intraductal Oncocytic Papillary Neoplasm of the Pancreas) [51]. The oldest manuscript within the 100 most cited manuscripts was published in 1994 by Sessa et al. (Intraductal papillary-mucinous tumors represent a distinct group of pancreatic neoplasms: an investigation of tumor cell differentiation and K-ras, p53 and c-erbB-2 abnormalities in 26 patients) [17].

The 100 most influential IPMN articles were published across 36 journals. The total number of articles per journal ranged from 1 to 13 (Table 2). The Annals of Surgery published the most articles and subsequently had most citations (n = 13 and 2889 citations). The journal with the highest impact factor (18.187) and highest five year impact factor (15.417) was Gastroenterology.

The United States of America was the country with most articles in the top 100 (n = 46), followed by Japan (n = 27) (Figure 1). The Johns Hopkins Medical Institute had the most articles in the top 100 (n = 11) and highest number of citations (n = 2383) (Table 3). Within the 100 most cited IPMN articles, 1 author had 5 and 2 authors had 3 first author publications.

One possible limitation of this study is that historical manuscripts may accumulate a higher number of citations despite lacking the impact of newer publications. In order to overcome the potential bias, the citation rate (number of citations divided by number of years since publication) was calculated for each article (Table 4). The citation rate for the top 10 articles ranged from 147 for Tanaka et al. (International consensus guidelines 2012 for the management of IPMN and MCN of the pancreas) [9] to 25 for Rodriguez et al. (Branch-Duct Intraductal Papillary Mucinous Neoplasms: Observations in 145 Patients Who Underwent Resection) [24]. USA had the most articles in the top 10 citation rate, closely followed by Japan.

Within the 100 most cited IPMN papers, management was the most frequently discussed topic (29 articles) (Table 5). Of which 14 articles were related to surgery and 9 articles focused on IPMN diagnosis. The second most common discussed topic was histology (18 of the top 100 papers). Seventeen articles reviewed IPMN prognosis. Fourteen papers reviewed the pathology of IPMN. Articles published prior to 2000, frequently published on the following topics: histology, etiology/pathophysiology and pathology of IPMN. However, this did differ when compared to papers published after 2006, where the most frequently published topics was management and prognosis of IPMN.
Table 1: The top 100 cited paper in IPMN

| Rank | Citations | First author          | Rank | Citations | First author          |
|------|-----------|-----------------------|------|-----------|-----------------------|
| 1    | 1006      | Tanaka, M[50]         | 51   | 127       | Lee, C[57]             |
| 2    | 737       | Tanaka, M[61]         | 52   | 127       | Brandwein, S[58]       |
| 3    | 546       | Hruban, R[10]         | 53   | 126       | Uehara, H[59]          |
| 4    | 526       | Sohn, T[11]           | 54   | 126       | Fernández-Cruz, L[60]  |
| 5    | 430       | Salvia, R[54]         | 55   | 125       | Tanno, S[54]           |
| 6    | 342       | Furukawa, T[31]       | 56   | 125       | Suzuki, Y[61]          |
| 7    | 324       | Zamboni, G[51]        | 57   | 125       | Traverso, L[62]        |
| 8    | 324       | Spinelli, K[13]       | 58   | 125       | Warshaw, A[64]         |
| 9    | 298       | Loftus, E[96]         | 59   | 124       | Matsubayashi, H[65]    |
| 10   | 292       | Sessa, F[72]          | 60   | 124       | Kubo, H[66]            |
| 11   | 291       | Chari, S[18]          | 61   | 122       | Nakamura, A[60]        |
| 12   | 286       | Sugiyama, M[69]       | 62   | 122       | Moore, P[68]           |
| 13   | 279       | Fernández-del Castillo, C[60] | 63   | 120       | Yamaguchi, K[69]       |
| 14   | 267       | Terris, B[31]         | 64   | 117       | Crippa, S[90]          |
| 15   | 247       | Canto, M[22]          | 65   | 116       | Falconi, M[71]         |
| 16   | 246       | Adsay, N[63]          | 66   | 114       | Shibahara, H[62]       |
| 17   | 246       | Rodríguez, J[54]      | 67   | 114       | Lüttges, J[63]         |
| 18   | 226       | Kobari, M[55]         | 68   | 113       | Poley, J[74]           |
| 19   | 223       | Sohn, T[30]           | 69   | 113       | Schnell dorfer, T[75]  |
| 20   | 222       | Schmidt, C[79]        | 70   | 113       | Sahani, D[86]          |
| 21   | 219       | D’Angelica, M[88]     | 71   | 112       | Yantiss, R[87]         |
| 22   | 217       | Kimura, W[90]         | 72   | 112       | Kitagawa, Y[88]        |
| 23   | 201       | Sugiyama, M[30]       | 73   | 112       | Doi, R[98]             |
| 24   | 183       | Thompson, L[15]       | 74   | 111       | Crippa, S[90]          |
| 25   | 180       | Lüttges, J[32]        | 75   | 110       | Biankin, AV[81]        |
| 26   | 177       | Terada, T[33]         | 76   | 108       | Fukushima, N[82]       |
| 27   | 179       | Zen, Y[54]            | 77   | 108       | Rivera, J[83]          |
| 28   | 179       | Adsay, N[61]          | 78   | 106       | Linder, J[84]          |
| 29   | 176       | Satoh, K[65]          | 79   | 105       | Tanaka, M[63]          |
| 30   | 167       | Maire, E[56]          | 80   | 104       | Mino-Kenudson, M[186]  |
| 31   | 167       | Adsay, N[57]          | 81   | 104       | Shyr, Y[87]            |
| 32   | 166       | Cellier, C[98]        | 82   | 102       | Sauvanet, A[88]        |
| 33   | 163       | Habbe, N[60]          | 83   | 101       | Taouli, B[92]          |
| 34   | 162       | Salvia, R[40]         | 84   | 101       | Sugiyama, M[60]        |
| 35   | 160       | Crippa, S[41]         | 85   | 101       | Fujii, H[61]           |
| 36   | 159       | Terris, B[42]         | 86   | 101       | Sugiyama, M[62]        |
| 37   | 157       | Pelaez-Luna, M[43]    | 87   | 100       | Fritz, S[93]           |
| 38   | 155       | Furukawa, T[44]       | 88   | 100       | Correa-Gallego, C[94]  |
| 39   | 155       | Z’graggen, K[45]      | 89   | 100       | House, M[91]           |
| 40   | 153       | Adsay, N[46]          | 90   | 100       | Adsay, N[63]           |
| 41   | 148       | Azar, C[47]           | 91   | 99        | Jang, J[74]            |
| 42   | 148       | Nagai, E[48]          | 92   | 99        | Wada, K[98]            |
| 43   | 147       | Sato, N[40]           | 93   | 98        | Abe, N[64]             |
| 44   | 144       | Brune, K[60]          | 94   | 97        | Horvath, K[100]        |
| 45   | 141       | Kallen, M[51]         | 95   | 96        | Klöppel, G[101]        |
| 46   | 137       | Koopmann, J[52]       | 96   | 95        | Del Chiaro, M[102]     |
| 47   | 136       | Sedlack, R[43]        | 97   | 94        | Li, A[100]             |
| 48   | 135       | Hara, T[54]           | 98   | 94        | Furukawa, T[84]        |
| 49   | 132       | Iacobuzio-Donahue, C[55] | 99   | 94        | Terada, T[53]          |
| 50   | 130       | Sato, N[68]           | 100  | 93        | Bernard, P[86]         |
DISCUSSION

Improvements in the histological classification of IPMN, accurate diagnostic radiological imaging algorithms and a further understanding of the impact of genetics on the pathophysiology of the disease represent 71% of the articles in this bibliometric analysis. This has resulted in the development of evidence based management protocols and improved risk stratification of patients with IPMN. This process improves the identification of patients for resection who will likely receive the greatest benefit.

Table 2: Journals with the top 100 cited IPMN papers

| Journal title                                | Impact Factor as of 2017 | 5 year Impact Factor | Number of manuscripts in the top 100 | Number of citations |
|----------------------------------------------|--------------------------|----------------------|--------------------------------------|--------------------|
| Annals of Surgery                            | 8.33                     | 8.57                 | 13                                   | 2889               |
| American Journal of Surgical Pathology      | 5.15                     | 4.59                 | 11                                   | 2152               |
| Gut                                          | 14.92                    | 12.75                | 8                                    | 1036               |
| American Journal of Pathology               | 4.21                     | 4.56                 | 5                                    | 669                |
| Archives of Surgery                          | 0.32                     | 3.56                 | 5                                    | 836                |
| American Journal of Gastroenterology        | 10.38                    | 9.04                 | 4                                    | 495                |
| Gastroenterology                             | 18.19                    | 15.42                | 4                                    | 970                |
| Gastrointestinal endoscopy                  | 6.22                     | 5.31                 | 4                                    | 535                |
| Pancreatology                                | 2.41                     | 2.21                 | 4                                    | 1963               |
| American Journal of Surgery                 | 2.40                     | 2.48                 | 3                                    | 321                |
| Journal of Gastrointestinal Surgery         | 2.81                     | 2.64                 | 3                                    | 365                |
| Surgery                                      | 3.31                     | 3.25                 | 3                                    | 315                |
| British Journal of Surgery                  | 5.60                     | 5.54                 | 2                                    | 402                |
| Cancer                                       | 3.50                     | 3.65                 | 2                                    | 355                |
| Cancer Research                              | 8.56                     | 8.74                 | 2                                    | 222                |
| Clinical Cancer Research                     | 8.74                     | 8.25                 | 2                                    | 231                |
| Clinical Gastroenterology and Hepatology    | 7.68                     | 6.88                 | 2                                    | 450                |
| Journal of Pathology                         | 7.38                     | 7.21                 | 2                                    | 216                |
| Pancreas                                     | 2.74                     | 2.81                 | 2                                    | 230                |
| Radiology                                    | 6.80                     | 6.39                 | 2                                    | 214                |
| Virchows Archiv: European Journal of Pathology | 2.65                  | 2.54                 | 2                                    | 634                |
| American Journal of Surgical Pathology      | 4.95                     | 4.78                 | 1                                    | 267                |
| Annals of Surgical Oncology                 | 3.66                     | 3.96                 | 1                                    | 99                 |
| Archives of Pathology & Laboratory Medicine | 2.63                     | 2.74                 | 1                                    | 141                |
| British Journal of Cancer                   | 5.57                     | 5.07                 | 1                                    | 122                |
| Cancer Biology & Therapy                    | 2.92                     | 3.11                 | 1                                    | 163                |
| Carcinogenesis                               | 4.87                     | 5.36                 | 1                                    | 100                |
| Digestive and Liver Disease                 | 2.72                     | 2.96                 | 1                                    | 95                 |
| Hepatogastroenterology                      | 0.79                     | 0.76                 | 1                                    | 96                 |
| Hepatology                                   | 11.71                    | 11.52                | 1                                    | 179                |
| Human Pathology                              | 2.79                     | 2.82                 | 1                                    | 108                |
| International Journal of Pancreatology      | 1.24                     | 1.29                 | 1                                    | 217                |
| Modern Pathology                             | 5.49                     | 5.10                 | 1                                    | 167                |
| Pathology International                      | 1.43                     | 1.57                 | 1                                    | 177                |
| Scientific Reports                           | 5.23                     | 4.41                 | 1                                    | 155                |
| Seminars in Diagnostic Pathology             | 1.96                     | 1.66                 | 1                                    | 100                |
| The Journal of Pathology                    | 7.38                     | 7.21                 | 1                                    | 206                |
Table 3: Institutions with the highest number of papers in the top 100

| Name of Institution                                    | Number of Publications in top 100 | Total number of citations |
|--------------------------------------------------------|----------------------------------|----------------------------|
| Johns Hopkins Medical Institutions                     | 11                               | 2383                       |
| Massachusetts General Hospital                         | 9                                | 1357                       |
| University of Verona                                   | 8                                | 1542                       |
| Kyorin University School of Medicine                   | 6                                | 912                        |
| Kyushu University                                      | 5                                | 2092                       |
| Mayo Clinic                                            | 4                                | 838                        |
| Karmanos Cancer Institute                              | 4                                | 666                        |
| Tohoku University School of Medicine                   | 3                                | 744                        |
| Virginia Mason Medical Center                          | 3                                | 336                        |
| University of Kiel                                     | 3                                | 390                        |
| Kagoshima University                                   | 2                                | 236                        |
| Memorial Sloan-Kettering Cancer Center                  | 2                                | 398                        |
| Tokyo Women’s Medical University                       | 2                                | 249                        |
| Hôpital Beaujon                                         | 2                                | 434                        |

Table 4: Top 10 IPMN papers with the highest citation rate

| Rank | Citation rate | First Author | Senior Author | Title                                                                 | Institution                      | Country |
|------|---------------|--------------|---------------|----------------------------------------------------------------------|-----------------------------------|---------|
| 1    | 147           | Tanaka, M    |               | International consensus guidelines 2012 for the management of IPMN and MCN of the pancreas | Kyushu University                | Japan   |
| 2    | 141           | Kallen, M    | Naini, B      | Intraductal Oncocytic Papillary Neoplasms of the Pancreas          | David Geffen School of Medicine  | USA     |
| 3    | 91            | Tanaka, M    |               | International consensus guidelines for management of intraductal papillary mucinous neoplasms and mucinous cystic neoplasms of the pancreas. | Kyushu University                | Japan   |
| 4    | 42            | Hruban, R    | Yonezawa, S   | An illustrated consensus on the classification of pancreatic Intraepithelial neoplasia and intraductal papillary mucinous neoplasms | Johns Hopkins Medical Institutions | USA     |
| 5    | 40            | Sohn, T      | Lillemoe, K   | Intraductal papillary mucinous neoplasms of the pancreas: an updated experience | Johns Hopkins Medical Institutions | USA     |
| 6    | 33            | Salvia, R    | Warshaw, A    | Main-duct intraductal papillary mucinous neoplasms of the pancreas: clinical predictors of malignancy and long-term survival following resection | University of Verona             | Italy   |
| 7    | 29            | Furukawa, T  | Yonezawa, S   | Classification of types of intraductal papillary-mucinous neoplasm of the pancreas: a consensus study | Tohoku University School of Medicine | Japan   |
| 8    | 26            | Furukawa, T  | Shiratori, K  | Whole-exome sequencing uncovers frequent GNAS mutations in intraductal papillary mucinous neoplasms of the pancreas | Tokyo Women’s Medical University | Japan   |
| 9    | 25            | Spinelli, K  | Pitt, H        | Cystic pancreatic neoplasms: observe or operate                      | Medical College of Wisconsin     | USA     |
| 10   | 25            | Rodriguez, J | Fernández-del Castillo, C | Branch-Duct Intraductal Papillary Mucinous Neoplasms: Observations in 145 Patients Who Underwent Resection | Harvard Medical School            | USA     |
Figure 1: A comparison of citations by country.

Table 5: Most frequently referenced topics *.

| Subject                        | Number of papers |
|--------------------------------|------------------|
| Management                     | 29               |
| Surgery                        | 14               |
| Histology                      | 18               |
| Prognosis                      | 17               |
| Pathology                      | 14               |
| Genetics                       | 14               |
| Aetiology/Pathophysiology      | 13               |
| Science                        | 13               |
| Diagnosis                      | 9                |
| Epidemiology                   | 2                |

*Several manuscripts had an overlap of topics, thus cell numbers do not add up to 100.

Publications with the highest levels of influence over the scientific community are theoretically much more likely to be cited. The subsequent citations form the foundation of the impact factor. The impact factor can be used as a proxy measure to identify journals with higher quality research and most influential manuscripts. The impact factor highlights the average citations of the article published within the journal during a predefined time period. The journals with the highest impact factor within this study are Gastroenterology, Gut and Hepatology (Impact Factor of 18.19, 14.92 and 11.711 respectively). The median impact factor of this study was 4.54 with 39% of the manuscripts published in journals with an impact factor less than 3.00. One proposed explanation for this is the impact of novelty of the findings of these articles. Novelty may be associated to science in general or only IPMN. Previously published findings established in other disease processes may then be reproduced and re-established in IPMN. It is unlikely that these original articles would be published in high impact factor journals. In the setting of this study these articles are considered likely to be influential.

Within this bibliometric analysis of the 100 most cited IPMN manuscripts, a variety of topics were covered. Histology of IPMN was the principle focus of 18 of the 100 most cited articles. Historically, diverse descriptive terminology was used to describe IPMN, thus causing diagnostic confusion. Recent advances in the histological analysis of IPMN have allowed the identification and subclassification of IPMN into 4 unique histopathological subtypes. These subtypes include oncocytic, gastric, pancreatobiliary and intestinal types [104]. The sub-classification is dependent on the immunophenotypes and cryoarchitectural features of the tumor. As a consequence of this sub-classification, we have a greater understanding of the malignant transformation potential of these tumors. This newly acquired knowledge influences our current treatment strategies and surveillance protocols for IPMN. Another important factor to consider is that these advances in histology permits correct identification of differential diagnoses of IPMN enabling the identification of benign tumors with a more favorable prognosis.

The definitive treatment for IPMN is surgery. However, surgery as a main topic of focus was only present in 17 of the 100 most cited papers and therefore is underrepresented in this study. Of the 17 papers that focussed on surgery, over half discussed novel surgical techniques for IPMN management, ranging from the role of laparoscopic surgery to techniques that preserve pancreatic parenchyma. Despite advances in surgical technique, pancreatic surgery remains to be associated with postoperative morbidity and mortality. A global change in the approach to pancreatic cystic tumor management has been noted. Historically, early aggressive surgery had been advocated. However as our understanding of the pathophysiology and the natural history of the disease have improved, surgery is reserved for patients’ with cystic tumors associated with high risk stigmata (dilated pancreatic duct, cyst >3cm, presence of high grade dysplasia) [107]. Surveillance protocols have been created by consensus of expert opinion that permit organized follow-up and monitoring of patients with IPMN who fail to meet the criteria for resection. This allows close observation for the development of concerning cystic features providing a good example of how advances in our understanding of the disease pathophysiology impacts and influences current management strategies.

There are study limitations within this manuscript. The main limitation is the potential for several types of bias, which in theory may affect the validity of the study results. English language bias, self-citation, powerful person bias and institutional bias may result in disproportionate citation. It is worth highlighting that older manuscripts are likely to collect more citations. An attempt has been made to overcome this potential bias through calculating the citation rate index. The most influential manuscripts may take several years to accumulate citations as a consequence of the publication lead-time for the citing manuscripts. Thus newly published articles with sufficient citations to be included in the top 100 contain useful and relevant information that have added importance to the
pre-existing literature regarding IPMN. Only the first and senior authors, and subsequently the institution of the first author was included in the analysis of this study. This represents another study limitation. It is likely that first authors would have collaborated and co-authored other manuscripts in the top 100 resulting in a under representation in the current study design.

CONCLUSION

This bibliometric analysis has highlighted the most cited IPMN manuscripts, which describe the pathophysiology of the disease and the current management strategies. Advances in our knowledge regarding the histology and prognosis of IPMN have influenced current practices. A paradigm shift has been observed from early aggressive surgery to the identification of patients with high risk cystic tumor features to establishing screening surveillance protocols to monitor the disease. The content of the 100 most cited manuscripts regarding IPMN demonstrated the diversity and the breadth of the newly acquired knowledge regarding IPMN over the last 23 years. This has resulted in improved treatment outcomes for patients with IPMN. The vast majority of these articles were published within journals with a recorded impact factor of less than 10, suggestive of an assumed lack of novelty to the general scientific community. This study not only identifies the most influential manuscripts in IPMN, it also creates a reference for both clinicians and scientific researchers who undertake research in the field of IPMN to what makes a citable paper. This study proposes that newer publications associated with higher citation rates, will significantly influence clinical practice and impact on the top 100 over the next 5 to 10 years.

REFERENCES

1. Goh BK. International guidelines for the management of pancreatic intraductal papillary mucinous neoplasms. World J Gastroenterol 2015 Sep 14;21(34):9833–7.
2. Machado NO, Al Qadhi H, Al Wahibi K. Intraductal papillary mucinous neoplasm of pancreas. N Am J Med Sci 2015 May;7(5):160–75.
3. Adsay NV, Conlon KC, Zee SY, Brennan MF, Klimstra DS. Intraductal papillary-mucinous neoplasms of the pancreas: An analysis of in situ and invasive carcinomas in 28 patients. Cancer 2002 Jan 1;94(1):62–77.
4. Kelly JC, Glynn RW, O’Brian DE, Felle P, McCabe JP. The 100 classic papers of orthopaedic surgery: A bibliometric analysis. J Bone Joint Surg Br 2010 Oct;92(10):1338–43.
5. Powell AG, Hughes DL, Wheat JR, Lewis WG. The 100 most influential manuscripts in gastric cancer: A bibliometric analysis. Int J Surg 2016 Apr;28:83–90.
6. Loonen MP, Hage JJ, Kon M. Plastic surgery classics: Characteristics of 50 top-cited articles in four plastic surgery journals since 1946. Plast Reconstr Surg 2008 May;121(5):320e–7e.
7. Paladugu R, Schein M, Gardezi S, Wise L. One hundred citation classics in general surgical journals. World J Surg 2002 Sep;26(9):1099–105.
8. Tanaka M, Chari S, Adsay V, Fernandez-del Castillo C, et al. International consensus guidelines for management of intraductal papillary mucinous neoplasms and mucinous cystic neoplasms of the pancreas. Pancreatology 2006;6(1–2):17–32.
9. Tanaka M, Fernández-del Castillo C, et al. International consensus guidelines 2012 for the management of IPMN and MCN of the pancreas. Pancreatology 2012 May-Jun;12(3):183–97.
10. Hruban RH, Takaori K, Klimstra DS, et al. An illustrated consensus on the classification of pancreatic intraepithelial neoplasia and intraductal papillary mucinous neoplasms. Am J Surg Pathol 2004 Aug;28(8):977–87.
11. Sohn TA, Yeo CJ, Cameron JL, et al. Intraductal papillary mucinous neoplasms of the pancreas: An updated experience. Ann Surg 2004 Jun;239(6):788–97; discussion 797–9.
12. Salvia R, Fernández-del Castillo C, et al. Main-duct intraductal papillary mucinous neoplasms of the pancreas: Clinical predictors of malignancy and long-term survival following resection. Ann Surg 2004 May;239(5):678–85; discussion 685–7.
13. Furukawa T, Klöppel G, Volkan Adsay N, et al. Classification of types of intraductal papillary-mucinous neoplasms of the pancreas: A consensus study. Virchows Arch 2005 Nov;447(5):794–9.
14. Zambroni G, Scarpa A, Bogina G, et al. Mucinous cystic tumors of the pancreas: Clinicopathological features, prognosis, and relationship to other mucinous cystic tumors. Am J Surg Pathol 1999 Apr;23(4):410–22.
15. Spinelli KS, Fromwiller TE, Daniel RA, et al. Cystic pancreatic neoplasms: Observe or operate. Ann Surg 2004 May;239(5):651–7; discussion 657–9.
16. Loftus EV Jr, Oliwares-Pakzad BA, Battis KP. Intraductal papillary-mucinous tumors of the pancreas: Clinicopathologic features, outcome, and nomenclature. Members of the Pancreas Clinic, and Pancreatic Surgeons of Mayo Clinic. Gastroenterology 1996 Jun;110(6):1909–18.
17. Sessa F, Solcia E, Capella C, et al. Intraductal papillary-mucinous tumours represent a distinct group of pancreatic neoplasms: An investigation of tumour cell differentiation and K-ras, pd3 and c-erbB-2 abnormalities in 26 patients. Virchows Arch 1994;425(4):357–67.
18. Chari ST, Yadav D, Smyrk TC, et al. Study of recurrence after surgical resection of intraductal papillary mucinous neoplasms of the pancreas. Gastroenterology 2002 Nov;123(5):1500–7.
19. Sugiyama M, Izumisato Y, Abe N, Masaki T, Mori T, Atomi Y. Predictive factors for malignancy in intraductal papillary-mucinous tumours of the pancreas. Br J Surg 2003 Oct;90(10):1244–9.
20. Fernández-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 Apr;138(4):427–3; discussion 433–4.
21. Terris B, Ponson P, Puy M, et al. Intraductal papillary mucinous tumors of the pancreas confined to secondary ducts show less aggressive pathologic features as compared with those involving the main pancreatic duct. Am J Surg Pathol 2000 Oct;24(10):1372–7.
22. Canto MI, Goggins M, Huban RH, et al. Screening for early pancreatic neoplasia in high-risk individuals: A prospective controlled study. Clin Gastroenterol Hepatol 2006 Jun;4(6):766–81; quiz 665.
23. Adsay NV, Merati K, Basturk O, et al. Pathologicallyand biologically distinct types of epithelium in intraductal papillary mucinous neoplasms: Delineation of an “intestinal” pathway of carcinogenesis in the pancreas. Am J Surg Pathol 2004 Jul;28(7):839–48.
24. Rodriguez JR, Salvia R, Crippa S, et al. Branch-duct intraductal papillary mucinous neoplasms: Observations in 145 patients who underwent resection. Gastroenterology 2007 Jul;133(1):72–9; quiz 309–10.
25. Kobari M, Egawa S, Shibuya K, et al. Intraductal papillary mucinous tumors of the pancreas comprise 2 clinical subtypes: Differences in clinical characteristics and surgical management. Arch Surg 1999 Oct;134(10):1131–6.
26. Sohn TA, Yeo CJ, Cameron JL, Iacobuzio-Donahue CA, Huban RH, Lillemoe KD. Intraductal papillary mucinous neoplasms of the pancreas: An increasingly recognized clinicopathologic entity. Ann Surg 2001 Sep;234(3):313–21; discussion 321–2.
27. Schmidt CM, White PB, Waters JA, et al. Intraductal papillary mucinous tumors of the pancreas: Predictors of malignant and invasive pathology. Ann Surg 2007 Oct;246(4):644–51; discussion 651–4.
28. D'Angelica M, Brennan MF, Suriawinata AA, Klimstra D, Conlon KC. Intraductal papillary mucinous neoplasms of the pancreas: An analysis of clinicopathologic features and outcome. Ann Surg 2004 Mar;239(3):400–8.
29. Kimura W, Nagai H, Kuroda A, Muto T, Esaki Y. Analysis of small cystic lesions of the pancreas. Int J Pancreatol 1995 Dec;18(3):197–206.
30. Sugiyama M, Atomi Y. Intraductal papillary mucinous tumors of the pancreas: Imaging studies and treatment strategies. Ann Surg 1998 Nov;228(5):685–91.
31. Thompson LD, Becker RC, Przygodzki RM, Adair CF, Heffess CS. Mucinous cystic neoplasm (mucinous cystadenocarcinoma of low-grade malignant potential) of the pancreas: A clinicopathologic study of 130 cases. Am J Surg Pathol 1999 Jan;23(1):1–16.
32. Lüttges J, Zamboni G, Longnecker D, Klöppel G. The immunohistochemical mucin expression pattern distinguishes different types of intraductal papillary mucinous neoplasms of the pancreas and determines their relationship to mucinous noncystic carcinoma and ductal adenocarcinoma. Am J Surg Pathol 2001 Jul;25(7):942–8.
33. Terada T, Kawaguchi M, Furukawa K, Sekido Y, Osamura Y. Minute mixed ductal-endocrine carcinoma of the pancreas with predominant intraductal growth. Pathol Int 2002 Nov;52(11):740–6.
34. Zen Y, Fujii T, Itatsu K, et al. Biliary papillary tumors share pathological features with intraductal papillary mucinous neoplasm of the pancreas. Hepatology 2006 Nov;44(5):1333–43.
35. Satoh K, Kaneko K, Hirota M, Masamune A, Satoh A, Shimosegawa T. Expression of survivin is correlated with cancer cell apoptosis and is involved in the development of human pancreatic ductal cell tumors. Cancer 2001 Jul;51(2):271–8.
36. Maires F, Hammel P, Terris B, et al. Prognosis of malignant intraductal papillary mucinous tumours of the pancreas after surgical resection. Comparison with pancreatic ductal adenocarcinoma. Gut 2002 Nov;51(5):717–22.
37. Adsay NV, Merati K, Andea A, et al. The dichotomy in the preinvasive neoplasia to invasive carcinoma sequence in the pancreas: Differential expression of MUC1 and MUC2 supports the existence of two separate pathways of carcinogenesis. Mod Pathol 2002 Oct;15(10):1087–95.
38. Cellier C, Cuillerier E, Palazzo L, et al. Intraductal papillary and mucinous tumors of the pancreas: Accuracy of preoperative computed tomography, endoscopic retrograde pancreatography and endoscopic ultrasonography, and long-term outcome in a large surgical series. Gastrointest Endosc 1998 Jan;47(1):42–9.
39. Habbe N, Koorstra JB, Mendell JT, et al. MicroRNA miR-155 is a biomarker of early pancreatic neoplasia. Cancer Biol Ther 2009 Feb;8(4):340–6.
40. Salvia R, Crippa S, Falconi M, et al. Branch-duct intraductal papillary mucinous neoplasms of the pancreas: To operate or not to operate? Gut 2007 Aug;56(8):1086–90.
41. Crippa S, Salvia R, Warshaw AL, et al. Mucinous cystic neoplasm of the pancreas is not an aggressive entity: lessons from 163 resected patients. Ann Surg 2008 Apr;247(4):571–9.
42. Terris B, Blaveri E, Crnogorac-Junecic T, et al. Characterization of gene expression profiles in intraductal papillary-mucinous tumors of the pancreas. Am J Pathol 2002 May;160(5):1745–54.
43. Pelaez-Luna M, Chari ST, Smyrk TC, et al. Do consensus indications for resection in branch duct intraductal papillary mucinous neoplasm predict malignancy? A study of 147 patients. Am J Gastroenterol 2007 Aug;102(8):1759–64.
44. Furukawa T, Kuboki Y, Tanji E, et al. Whole-exome sequencing uncovers frequent GNAS mutations in intraductal papillary mucinous neoplasms of the pancreas. Sci Rep 2011;1:161.
45. Z’graggen K, Rivera JA, Compton CC, et al. Prevalence of activating K-ras mutations in the evolutionary stages of neoplasia in intraductal papillary mucinous tumors of the pancreas. Ann Surg 1997 Oct;226(4):491–8; discussion 498–500.
46. Adsay NV, Pierson C, Sarkar F, et al. Colloid (mucinous noncystic) carcinoma of the pancreas. Am J Surg Pathol 2001 Jan;25(1):26–42.
47. Azar C, Van de Stadt J, Rickaert F, et al. Intraductal papillary mucinous tumours of the pancreas. Clinical and therapeutic issues in 32 patients. Gut 1996 Sep;39(3):457–64.
48. Nagai E, Ueki T, Chijiwa K, Tanaka M, Tsumeyoshi M. Intraductal papillary mucinous neoplasms of the pancreas associated with so-called “mucinous duct ectasia”. Histochemical and immunohistochemical analysis of 29 cases. Am J Surg Pathol 1995 May;19(5):576–89.

49. Sato N, Rosty C, Jansen M, et al. STK11/LKB1 Peutz-Jeghers gene inactivation in intraductal papillary-mucinous neoplasms of the pancreas. Am J Pathol 2001 Dec;159(6):2017–22.

50. Brune K, Abe T, Canto M, et al. Multifocal neoplastic precursor lesions associated with lobular atrophy of the pancreas in patients having a strong family history of pancreatic cancer. Am J Surg Pathol 2006 Sep;30(9):1067–76.

51. Kallen ME, Naini BV. Intraductal Oncocytic Papillary Neoplasms of the Pancreas. Arch Pathol Lab Med 2016 Sep;140(9):992–6.

52. Koopmann J, Bauckhauts P, Brown DA, et al. Serum macrophage inhibitory cytokine 1 as a marker of pancreatic and other peripancreatic cancers. Clin Cancer Res 2004 Apr;11(7):2386–92.

53. Sedlack R, Affi A, Vazquez-Sequeiros E, Norton ID, Clain JE, Wiersema MJ. Utility of EUS in the evaluation of cystic pancreatic lesions. Gastrointest Endosc 2002 Oct;56(4):543–7.

54. Haras T, Yamaguchi T, Ishihara T, et al. Diagnosis and patient management of intraductal papillary-mucinous tumor of the pancreas by using peroral pancreatoscopy and intraductal ultrasonography. Gastroenterology 2002 Jan;122(1):34–43.

55. Iacobuzio-Donahue CA, Klimstra DS, Adsay NV, et al. The mucin profile of noninvasive and invasive ductal adenocarcinomas. Am J Pathol 2000 Sep;157(3):755–61.

56. Sato N, Fukushima N, Maitra A, et al. Gene expression profiling identifies genes associated with invasive intraductal papillary mucinous neoplasms of the pancreas. Am J Pathol 2004 Mar;164(3):903–14.

57. Lee CJ, Scheiman J, Anderson MA, et al. Risk of malignancy in resected cystic tumors of the pancreas < or =3 cm in size: Is it safe to observe asymptomatic patients? A multi-institutional report. J Gastrointest Surg 2008 Feb;12(2):234–42.

58. Brandwein SL, Farrell JJ, Centeno BA, Brugge WR. Detection and tumor staging of malignancy in cystic, intraductal, and solid tumors of the pancreas by EUS. Gastrointest Endosc 2001 Jun;53(7):722–7.

59. Uehara H, Nakazumi M, Ishikawa O, et al. Assessment of ductal carcinoma of the pancreas during follow-up of branch duct intraductal papillary mucinous neoplasm of the pancreas. Gut 2008 Nov;57(11):1561–5.

60. Fernández-Cruz L, Cosa R, Blanco L, Levi S, López-Boado MA, Navarro S. Curative laparoscopic resection for pancreatic neoplasms: A critical analysis from a single institution. J Gastrointest Surg 2007 Dec;11(12):1607–21; discussion 1621–2.

61. Tanno S, Nakano Y, Nishikawa T, et al. Natural history of branch duct intraductal papillary-mucinous neoplasms of the pancreas without mural nodules: Long-term follow-up results. Gut 2008 Mar;57(3):339–43.

62. Suzuki Y, Atomi Y, Sugiyama M, et al. Cystic neoplasm of the pancreas: A Japanese multiinstitutional study of intraductal papillary mucinous tumor and mucinous cystic tumor. Pancreas 2004 Apr;28(3):241–6.

63. Traverso LW, Peralta EA, Ryan JA Jr, Kozarek RA. Intraductal neoplasms of the pancreas. Am J Surg 1998 May;175(5):426–32.

64. Warshaw AL, Rattner DW, Fernández-del Castillo C, Z'graggen K. Middle segment pancreatectomy: A novel technique for conserving pancreatic tissue. Arch Surg 1998 Mar;133(3):327–31.

65. Matsubayashi H, Canto M, Sato N, et al. DNA methylation alterations in the pancreatic juice of patients with suspected pancreatic disease. Cancer Res 2006 Jan 15;66(2):1208–17.

66. Kubo H, Chijiiwa Y, Akahoshi K, et al. Intraductal papillary-mucinous tumors of the pancreas: Differential diagnosis between benign and malignant tumors by endoscopic ultrasonography. Am J Gastroenterol 2001 May;96(5):1429–34.

67. Nakamura A, Horinouchi M, Goto M, et al. New classification of pancreatic intraductal papillary-mucinous tumor by mucin expression: Its relationship with potential for malignancy. J Pathol 2002 Jun;197(2):201–10.

68. Moore PS, Orlandini S, Zamboni G, et al. Pancreatic tumours: Molecular pathways implicated in ductal cancer are involved in apolipoprotein B not in exocrine nonductal or endocrine tumorigenesis. Br J Cancer 2001 Jan;84(2):253–62.

69. Yamaguchi K, Ohutsuka T, Nakaoka K, Tanaka M. Intraductal papillary-mucinous tumor of the pancreas concomitant with ductal carcinoma of the pancreas. Pancreatology 2002;2(5):84–90.

70. Crippa S, Bassi C, Warshaw AL, et al. Middle pancreatoduodenectomy: Indications, short- and long-term operative outcomes. Ann Surg 2007 Jul;246(1):69–76.

71. Falconi M, Salvia R, Bassi C, Zamboni G, Talamini G, Pederzoli P. Clinicopathological features and treatment of intraductal papillary mucinous tumour of the pancreas. Br J Cancer 2001 Mar;84(2):253–62.

72. Shibahara H, Tamada S, Goto M, et al. Pathologic features of mucin-producing bile duct tumors: Two histopathologic categories as counterparts of pancreatic intraductal papillary-mucinous neoplasms. Am J Surg Pathol 2004 Mar;28(3):327–38.

73. Lüttges J, Feyerabend B, Buchelt T, Pacena M, Köppel G. The mucin profile of noninvasive and invasive mucinous cystic neoplasms of the pancreas. Am J Surg Pathol 2002 Apr;26(4):466–71.

74. Polev JW, Kluitj J, Gouma DJ, et al. The yield of first-time endoscopic ultrasonography in screening individuals at a high risk of developing pancreatic cancer. Am J Gastroenterol 2009 Sep;104(9):2175–81.

75. Schnelldorfer T, Sarr MG, Nagorney DM, et al. Experience with 208 resections for intraductal papillary mucinous neoplasm of the pancreas. Arch Surg 2008 Jul;143(7):639–46; discussion 646.

76. Sahani DV, Kadavigere R, Blake M, Fernandez-Del Castillo C, Lauwers GY, Hahn PF. Intraductal papillary mucinous neoplasm of pancreas: Multi-detector row CT with 2D curved reformations–correlation with MRCP. Radiology 2006 Feb;238(2):560–9.
91. Fujii H, Inagaki M, Kasai S, et al. Genetic progression and heterogeneity in intraductal papillary-mucinous neoplasms of the pancreas. Am J Pathol 1997 Nov;151(5):1447–54.

92. Sugiyama M, Atomi Y, Kuroda A. Two types of mucin-producing cystic tumors of the pancreas: Diagnosis and treatment. Surgery 1997 Sep;122(3):617–25.

93. Fritz S, Klauss M, Bergmann F, et al. Small (Sendai negative) branch-duct IPMNs: Not harmless. Ann Surg 2012 Aug;256(2):313–20.

94. Correa-Gallego C, Ferrone CR, Thayer SP, Wargo JA, Warshaw AL, Fernández-Del Castillo C. Incidental pancreatic cysts: Do we really know what we are watching? Pancreatology 2010;10(2–3):144–50.

95. House MG, Guo M, Iacobuzio-Donahue C, Herman JG. Molecular progression of promoter methylation in intraductal mucinous neoplasms (IPMN) of the pancreas. Carcinogenesis 2003 Feb;24(2):193–8.

96. Adsay NV, Longnecker DS, Klimstra DS. Pancreatic tumors with cystic dilatation of the ducts: Intraductal papillary mucinous neoplasms and intraductal oncocytic papillary neoplasms. Semin Diagn Pathol 2000 Feb;17(1):16–30.

97. Jang JY, Kim SW, Lee SE, et al. Treatment guidelines for branch duct type intraductal papillary mucinous neoplasms of the pancreas: When can we operate or observe? Ann Surg Oncol 2008 Jan;15(1):199–205.

98. Wada K, Kozarek RA, Traverso LW. Outcomes following resection of invasive and noninvasive intraductal papillary mucinous neoplasms of the pancreas. Am J Surg 2005 May;189(5):632–6; discussion 637.

99. Abe N, Watanabe T, Masaki T, et al. Pancreatic duct cell carcinomas express high levels of high mobility group 1(Y) proteins. Cancer Res 2000 Jun 15;60(12):3117–22.

100. Horvath KD, Chabot JA. An aggressive resectional approach to cystic neoplasms of the pancreas. Am J Surg 1999 Oct;178(4):269–74.

101. Klöppel G. Clinicopathologic view of intraductal papillary-mucinous tumor of the pancreas. Hepatogastroenterology 1998 Nov–Dec;45(24):1981–5.

102. Del Chiaro M, Verbeke C, Salvia R, et al. European experts consensus statement on cystic tumours of the pancreas. Dig Liver Dis 2013 Sep;45(9):703–11.

103. Li A, Yu J, Kim H, et al. MicroRNA array analysis finds elevated serum miR-1290 accurately distinguishes patients with low-stage pancreatic cancer from healthy and disease controls. Clin Cancer Res 2013 Jul 1;19(13):3600–10.

104. Furukawa T, Hatori T, Fujita I, et al. Prognostic relevance of morphological types of intraductal papillary mucinous neoplasms of the pancreas. Gut 2011 Apr;60(4):509–16.

105. Terada T, Ohta T, Sasaki M, Nakamura Y, Kim YS. Expression of MUC apomucins in normal pancreas and pancreatic neoplasms. J Pathol 1996 Oct;180(2):160–5.

106. Bernard P, Scoazec JY, Joubert M, et al. Intraductal papillary mucinous tumors: When can we operate or observe? Ann Surg Oncol 2008 Jan;15(1):199–205.

107. Karoumpalis I, Christodoulou DK. Cystic lesions of the pancreas. Ann Gastroenterol 2016 Apr–Jun;29(2):155–61.
**Author Contributions**
Daniel Hughes – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Ioan Hughes – Acquisition of data, Analysis and interpretation of data, Drafting the article, Final approval of the version to be published
Arfon GMT Powell – Substantial contributions to conception and design, Analysis and interpretation of data, Drafting the article, Final approval of the version to be published
Bilal Al-Sarireh – Analysis and interpretation of data, Drafting the article, Final approval of the version to be published

**Guarantor of Submission**
The corresponding author is the guarantor of submission.

**Source of Support**
None

**Conflict of Interest**
Authors declare no conflict of interest.

**Copyright**
© 2018 Daniel Hughes et al. This article is distributed under the terms of Creative Commons Attribution License which permits unrestricted use, distribution and reproduction in any medium provided the original author(s) and original publisher are properly credited. Please see the copyright policy on the journal website for more information.