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ORIGINAL ARTICLE

First world consensus conference on pancreas transplantation: Part I—Methods and results of literature search

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Comprehensive evidence-based guidelines for the practice of pancreas transplantation are yet to be established. The First World Consensus Conference on Pancreas Transplantation was convened for this purpose. A steering committee selected the participants and defined the questions to be addressed. A group of literature reviewers identified 597 studies to be included in summaries for guidelines production. Expert groups formulated the first draft of recommendations. Two rounds of discussion and voting occurred online, using the Delphi method (agreement rate ≥85%). After each round, critical responses of experts were reviewed, and recommendations were amended accordingly. Recommendations were finalized after live discussions. Each session was preceded by expert presentations and a summary of results of systematic literature review. Up to three voting rounds were allowed for each recommendation. To avoid potential conflicts of interest, deliberations on issues regarding the impact of pancreas transplantation on the management of diabetes were conducted by an independent jury. Recommendations on technical issues were determined by experts and validated using the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument. Quality of evidence was assessed using the Scottish Intercollegiate Guidelines Network (SIGN) methodology. Each recommendation received a GRADE rating (Grading of Recommendations, Assessment, Development and Evaluations).

KEYWORDS
clinical research / practice, diabetes, pancreas / simultaneous pancreas-kidney transplantation, survey

Abbreviations: AGREE II, appraisal of guidelines for research and evaluation II; CMV, cytomegalovus; CNI, calcineurin inhibitors; DBD, donation after brainstem death; eGFR, estimated glomerular filtration rate; GRADE, grading of recommendations, assessment, development, and evaluations; PAK, pancreas after kidney transplant; HTK, histidine-tryptophan-ketoglutarate; MFI, mean fluorescent intensity; DSA, donor specific antibodies; PICO, population, intervention, comparison, outcomes; PTA, pancreas transplant alone; SIGN, Scottish Intercollegiate Guidelines Network; SPK, simultaneous pancreas and kidney.

Piero Marchetti, Raja Kandaswamy and Thierry Berney are all senior authors.

1 | INTRODUCTION

Vascularized pancreas transplantation is a complex surgical procedure for which significant progress has been made over the past 55 years. The team of Lillehei and Kelly performed the first simultaneous pancreas and kidney (SPK) transplant at the University of Minnesota in 1966.[1] Pancreas transplantation is now a commonly performed procedure offered most often in the context of an SPK transplant for advanced diabetic nephropathy. Alternatively, pancreas transplantation may be performed as a sequential pancreas after kidney (PAK) transplant if the kidney transplant is performed first, usually from a living donor. Less often, a pancreas transplant alone (PTA) may be performed in patients with diabetes who have preserved renal function but other life-threatening complications of diabetes, particularly hypoglycemia unawareness.[2] With advances in surgical techniques, immunosuppression, and preservation technology, outcomes have improved significantly. There still remain many unanswered questions regarding several aspects of pancreas transplantation, including donor and recipient selection, selection of optimal procedure, organ procurement, preservation techniques, and ideal immunosuppression. Despite the publication of several guidelines focusing on specific aspects of pancreas transplantation,[3-7] to date there has not been a forum in which the international transplant community has convened to perform a comprehensive assessment of the value of pancreas transplantation and deliberate on evidence-based guidelines. To this end, the First World Consensus Conference on Pancreas Transplantation was held in Pisa, Italy, from October 17 to October 19, 2019.

We herein describe the methods used for the Consensus and provide the results of the literature search (Part I). Approved statements are provided in a separate document in this supplement of the journal (Part II).

2 | AIMS

The purpose of the First World Consensus Conference on Pancreas Transplantation was to provide evidence-based guidelines for clinical practice of pancreas transplantation. Additionally, the impact of SPK, PAK, and PTA was independently assessed by an external jury with the purpose of defining the role of pancreas transplantation in the modern management of diabetes.

This consensus conference does not aim to address any issues related to islet transplantation, either as a stand-alone therapy or as an alternative treatment option to pancreas transplantation.

3 | METHODS

The First World Consensus Conference on Pancreas Transplantation was supported by the International Pancreas and Islet Transplant Association (IPITA) and was organized under the auspices of the European Society for Organ Transplantation, the European Association for the Study of Diabetes, the Italian Society for Organ Transplantation, The Italian Society of Surgery, the Italian Society of Diabetology, the Italian Association of Diabetologists, and the Italian Society of Endocrinology. The consensus conference was also endorsed by the Italian Prime Minister's Office, the Italian Ministry of Health, the Tuscany Region, and the City of Pisa.

The consensus conference received no funds from private companies. Costs were largely covered by a main unrestricted grant from Fondazione Pisa (https://www.fondazionepisa.it/). Additional financial support was obtained from Tuscany Region, University of Pisa, and Pisa University Hospital. There was also an economic contribution from registration fees. Industries were not involved in any step of the consensus, and no representative of commercial companies was involved in any committee, jury, expert panel, or literature review groups. No participant received an honorarium. Travel expenses were covered by modest preset amounts based on the distance to travel to the meeting. Lodging expenses were covered for all participants.

The consensus involved a steering committee, a jury, a group of experts, a validation committee, and a group of literature reviewers. Two experts in validation procedures (Federica Cipriani and Mario Miccoli) were also involved in supporting the work of the validation committee to ensure strict adherence to the Appraisal of Guidelines for Research and Evaluation II (AGREE II).[8] All experts were asked to take a tutorial on the Scottish Intercollegiate Guidelines Network (SIGN) method,[9] which includes the grading of recommendations, assessment, development, and evaluations (GRADE) methodology.[10]

The steering committee was composed of Thierry Berney (surgeon, University of Geneva), Ugo Boggi (surgeon, University of Pisa), Raja Kandaswamy (surgeon, University of Minnesota), Piero Marchetti (endocrinologist, University of Pisa), and Fabio Vistoli (surgeon, University of Pisa). A list of members of the jury, experts, validation committee, and literature reviewers is provided in Table 1. Overall, 76 people were involved, representing 17 countries and 5 continents.

3.1 | Consensus conference format

Through a series of online meetings and discussions, the steering committee identified the main topics that needed to be covered in the consensus and defined relevant questions for each topic. Questions, whenever possible, were proposed in PICO style (population, intervention, comparison, outcomes). A total of 12 main topics and 144 questions were defined.

The 12 main topics were categorized in two key domains. First, the impact of SPK, PAK, and PTA on management of patients with diabetes (three topics for a total of 35 questions), as depicted in Table 2. Second, technical issues related to practice of pancreas transplantation (nine topics for a total of 109 questions), as shown in Table 3. To maintain objectivity, the overall impact of SPK, PAK, and PTA was defined by an independent jury and not by professionals holding potential interests in these treatments (e.g., pancreas transplant surgeons), while technical issues related to the practice of pancreas transplantation were evaluated by those who actually perform these procedures. The impact of SPK, PAK, and PTA on the management of

TABLE 1 Members of steering committee, jury, expert group, validation committee, and literature reviewers

	Name	Field of interest	Affiliation	City	Country
Steering committee					
	Berney Thierry	Surgery	University of Geneva	Geneva	Switzerland
	Boggi Ugo	Surgery	University of Pisa	Pisa	Italy
	Kandaswamy Raja	Surgery	University of Minnesota	Minneapolis, MN	United States
	Marchetti Piero	Endocrinology/ diabetes	University of Pisa	Pisa	Italy
	Vistoli Fabio	Surgery	University of Pisa	Pisa	Italy
Jury					
	Cardillo Massimo	Immunogenetics	Centro Nazionale Trapianti	Rome	Italy
	Cupisti Adamasco	Nephrology	University of Pisa	Pisa	Italy
	Ettorre Giuseppe Maria	Surgery	S. Camillo Hospital	Rome	Italy
	Gruessner Angelika C.	Epidemiology/ statistics	Downstate University	New York, NY	United States
	Gunton Jenny E.	Endocrinology/ diabetes	University of Sydney	Sydney	Australia
	Menichetti Francesco	Infective diseases	University of Pisa	Pisa	Italy
	Robertson R. Paul	Endocrinology/ diabetes	University of Washington	Seattle, WA	United States
	Ross Lainie F.	Bioethics	University of Chicago	Chicago, IL	United States
	Rossi Massimo	Surgery	University of Rome - Umberto I	Rome	Italy
Expert group					
	Bartlett Stephen T.	Surgery	OSF Cardiovascular Institute	Rockford, IL	United States
	Benedetti Enrico	Surgery	University of Illinois at Chicago	Chicago, IL	United States
	Burke George W. 3rd	Surgery	University of Miami	Miami, FL	United States
	Casanova Daniel	Surgery	University of Santander	Santander	Spain
	Cooper Matthew	Surgery	Medstar Georgetown Transplant Institute	Washington, DC	United States
	de Koning Eelco J.P.	Endocrinology/ diabetes	University of Leiden	Leiden	The Netherlands
	Drachenberg Cinthia	Pathology	University of Maryland	Baltimore, MD	United States
	Fernandez Cruz Laureano	Surgery	University of Barcelona	Barcelona	Spain
	Fridell Jonathan A.	Surgery	University of Indiana	Indianapolis, IN	United States
	Friend Peter J.[a]	Surgery	University of Oxford	Oxford, England	United Kingdom
	Gaber Osama A.[a]	Surgery	Weill Cornell Medical College	Houston, TX	United States
	Gruessner Rainer W.G.	Surgery	Downstate University	New York, NY	United States
	Han Duck-Jong	Surgery	University of Seoul	Seoul	South Korea
	Kaufman Dixon	Surgery	University of Wisconsin	Madison, WI	United States
	Kenmochi Takashi[a]	Surgery	Fujita Health University	Nagoya, Aichi	Japan
	Oberholzer Jose	Surgery	University of Virginia	Charlottesville, VA	United States
	Odorico Jon S.	Surgery	University of Wisconsin	Madison, WI	United States
	Öllinger Robert	Surgery	University of Berlin	Berlin	Germany
	Perosa Marcelo	Surgery	Leforte Hospital Sao Paulo	Sao Paulo	Brazil
	Pleass Henry	Surgery	University of Sydney	Sydney	Australia
	Rigotti Paolo[a]	Surgery	University of Padua	Padua	Italy

(Continues)

TABLE 1 (Continued)

	Name	Field of interest	Affiliation	City	Country
	Saudek Frantisek	Endocrinology/ diabetes	Institute for Clinical and Experimental Medicine	Prague	Czech Republic
	Schenker Peter	Surgery	University of Bochum	Bochum	Germany
	Secchi Antonio[a]	Endocrinology/ diabetes	University Vita-Salute - S. Raffaele Hospital	Milan	Italy
	Stock Peter G.	Surgery	University of California at San Francisco	San Francisco, CA	United States
	Stratta Robert J.[a]	Surgery	Wake Forest School of Medicine	Winston-Salem, NC	United States
	Watson Christopher C.E.[a]	Surgery	University of Cambridge	Cambridge, England	United Kingdom
	White Steven A.	Surgery	Newcastle University	Newcastle upon Tyne, England	United Kingdom
Validation committee					
	Cipriani Federica	Surgery	University Vita-Salute - S. Raffaele Hospital	Milan	Italy
	Miccoli Mario	Statistics	University of Pisa	Pisa	Italy
	Arbogast Helmut P.	Surgery	University of Munich	Munich	Germany
	Badet Lionel	Surgery	University of Lyon	Lyon	France
	Caldara Rossana	Nephrology	University Vita-Salute - S. Raffaele Hospital	Milan	Italy
	Davide Josè	Surgery	University of Porto	Porto	Portugal
	Donzilia Sousa Silva	Surgery	University of Porto	Porto	Portugal
	Langer Robert M.	Surgery	University of Linz	Linz	Austria
	Maffi Paola	Endocrinology/ diabetes	University Vita-Salute - S. Raffaele Hospital	Milan	Italy
	Marselli Lorella	Endocrinology/ diabetes	University of Pisa	Pisa	Italy
	Morelon Emmanuel	Nephrologist	University of Lyon	Lyon	France
	Oniscu Gabriel	Surgery	University of Edinburgh	Edinburgh, Scotland	United Kingdom
	Orlando Giuseppe	Surgery	Wake Forest School of Medicine	Winston-Salem, NC	United States
	Socci Carlo	Surgery	University Vita-Salute - S. Raffaele Hospital	Milan	Italy
	Squifflet Jean Paul	Surgery	University of Liege	Liege	Belgium
	Uva Pablo	Surgery	Institution of Transplants and High Complexity	Buenos Aires	Argentina
Literature reviewers					
	Andres Axel	Surgery	University of Geneva	Geneva	Switzerland
	Baronti Walter	Endocrinology/ diabetes	University of Pisa	Pisa	Italy
	Branchereau Julien	Surgery	University of Nantes	Nantes	France
	Buron Fanny	Nephrology	University of Lyon	Lyon	France
	Furian Lucrezia	Surgery	University of Padua	Padua	Italy
	Iacopi Sara	Surgery	University of Pisa	Pisa	Italy
	Kauffmann Emanuele Federico	Surgery	University of Pisa	Pisa	Italy
	Khambalia Hussein A.	Surgery	University of Manchester	Manchester, England	United Kingdom

(Continues)

TABLE 1 (Continued)

	Name	Field of interest	Affiliation	City	Country
	Lai Quirino	Surgery	University of Rome - Umberto I	Rome	Italy
	Mittal Shruti	Surgery	University of Oxford	Oxford, England	United Kingdom
	Napoli Niccolò	Surgery	University of Pisa	Pisa	Italy
	Neri Flavia	Surgery	University of Padua	Padua	Italy
	Ortenzi Monica	Surgery	University of Ancona	Ancona	Italy
	Perrone Vittorio Grazio	Surgery	University of Pisa	Pisa	Italy
	Redfield Robert R.	Surgery	University of Wisconsin	Madison, WI	United States
	Ricci Claudio	Surgery	University of Bologna	Bologna	Italy
	Scalea Joseph R.	Surgery	University of Maryland	Baltimore, MD	United States
	Terrenzio Chiara	Endocrinology/ diabetes	University of Pisa	Pisa	Italy

[a]These authors participated only to online Delphi rounds.

patients with diabetes was assessed using the Zurich–Danish model (Table 4).[11] This model charges a jury with the duty to approve deliberations. The jury receives relevant information from expert groups, participates into audience discussions, asks questions to experts, and calls for an audience vote on proposed statements, but independently draws the final deliberations. Members of the jury have to be free from any potential conflict of interest with the topic to be evaluated.

In contrast, recommendations on technical issues were approved by a panel of experts in pancreas transplantation and were validated by a distinct group of experts using the AGREE II instrument.[8] This consensus format has been used several times to address technical issues concerning surgical procedures, and results have been reported in high-impact journals.[12,13]

For each question, the following actions were undertaken:

1. **A systematic literature review**. The search strategy followed guidelines outlined in the Cochrane Handbook for Systematic Reviews of Interventions and was reported according to the Preferred Reporting Items for Systematic Reviews.[14,15] Relevant studies were identified using PubMed, Embase, and Cochrane databases. Other studies identified by cross-referencing were also retrieved and reviewed. The following exclusion criteria were adopted: first, documents published in a format other than full-text peer-reviewed scientific article (e.g., abstracts from scientific meetings and book chapters); second, case reports; third, letters not containing original research data; fourth, articles not published in English; and fifth, articles from the same institution or research group. In this case, only the most recent contribution was considered, to avoid data overlap. Quality of evidence was assessed using the SIGN methodology.[9] All literature searches were conducted from January 1, 1967 to the closest possible date to the consensus conference in 2019.
2. **A summary of available studies**. A sorted summary was prepared to answer each question and was included in evidence tables.
3. **A proposed recommendation for each question**. This included a GRADE rating (Tables 5 and 6).
4. **A proposed action**. This aimed to provide suggestions for future research.

Proposed recommendations were distributed online to all experts, for a first Delphi vote[16] using Google Modules. A space for feedback comments was also provided, so that if a recommendation was not approved (agreement rate ≥85%), the steering committee could draw a new proposal incorporating criticisms. Amended recommendations were then sent back to the experts for a second online Delphi vote. All responses were kept anonymous. All recommendations were discussed again at the consensus conference for final approval.

The general structure of the consensus conference is summarized in Figure 1.

3.2 | Participants

A participant list for the First World Consensus Conference on Pancreas Transplantation was finalized by a nomination and voting process within the steering committee.

Jury members were identified among highly reputable endocrinologists (GJE and RRP), nephrologists (CA), transplant surgeons without direct involvement in pancreas transplantation (EGM and RM), epidemiologists (GAC) and biostatistics, experts in organ allocation (CM), infectious disease specialists (MF), and ethicists (RLF). Jury members were also chosen based on expertise in clinical research methods.

Experts were selected based on their international reputation and contribution to the medical literature on pancreas transplantation for each of the identified topics.

Junior literature reviewers were identified according to proposals received from experts, based on known research interest and experience with literature search and review.

Expert groups and junior literature reviewers were defined in October 2018. Each group received a list of topics to address and

TABLE 2 Questions on impact of SPK, PAK, and PTA

A. Impact of simultaneous pancreas-kidney transplantation (SPK)
A.1 In suitable recipients, does an SPK transplant increase life expectancy or improve quality of life?
A.2 In suitable SPK recipients with type 1 diabetes, does an SPK transplant improve life-expectancy or quality of life?
A.3 In suitable SPK recipients with type 2 diabetes, does an SPK transplant improve life-expectancy or quality of life?
A.4 In patients with type 1 diabetes and end-stage renal disease on dialysis, does an SPK transplant increase longevity or improve quality of life?
A.5 In patients with type 1 diabetes and end-stage renal disease on dialysis, does an SPK transplant increase longevity or improve quality of life compared to live donor kidney transplantation?
A.6 In patients with type 1 diabetes and end-stage renal disease on dialysis, does an SPK transplant increase longevity or improve quality of life compared to live donor kidney transplantation with islet cell transplantation?
A.7 In patients with type 1 diabetes and end-stage renal disease on dialysis, does an SPK transplant increase longevity or improve quality of life compared to deceased donor kidney transplantation?
A.8 In patients with type 1 diabetes and end-stage renal disease on dialysis, does an SPK transplant increase longevity or improve quality of life compared to deceased donor kidney transplantation with islet cell transplantation?
A.9 In pre-emptive SPK recipients with type 1 diabetes, does an SPK transplant improve longevity or quality of life?
A.10 In pre-emptive SPK recipients with type 1 diabetes, does an SPK transplant improve longevity or quality of life compared to live donor kidney transplantation?
A.11 In pre-emptive SPK recipients with type 1 diabetes, does an SPK transplant improve longevity or quality of life compared to live donor kidney transplantation with islet cell transplantation?
A.12 In pre-emptive SPK recipients with type 1 diabetes, does an SPK transplant improve longevity or quality of life compared to deceased donor kidney transplantation?
A.13 In pre-emptive SPK recipients with type 1 diabetes, does an SPK transplant improve longevity or quality of life compared to deceased donor kidney transplantation with islet cell transplantation?
A.14 In patients with type 2 diabetes and end-stage renal disease on dialysis, does an SPK transplant improve quality of life or increase longevity?
A.15 In patients with type 2 diabetes and end-stage renal disease on dialysis, does an SPK transplant improve quality of life or increase longevity compared to live donor kidney transplantation?
A.16 In patients with type 2 diabetes and end-stage renal disease on dialysis, does an SPK transplant improve quality of life or increase longevity compared to deceased donor kidney transplantation?
A.17 In preemptive recipients with type 2 diabetes, does an SPK transplant improve quality of life or increase longevity compared to current medical therapy?
A.18 In preemptive recipients with type 2 diabetes, does an SPK transplant improve quality of life or increase longevity compared to live donor kidney transplantation?
A.19 In preemptive recipients with type 2 diabetes, does an SPK trasnplant improve quality of life or increase longevity compared to deceased donor kidney transplantation?
B. Impact of pancreas after kidney transplantation (PAK)
B.1 In suitable PAK recipients, is PAK transplant associated with additional risks? What is the risk of death compared to current medical therapies?
B.2 In suitable PAK recipients with type 1 diabetes, does PAK prolong life or improve quality of life compared to current diabetes therapy?
B.3 In suitable PAK recipients with type 1 diabetes who received a live donor kidney, does PAK transplant increase life expectancy or improve quality of life?
B.4 In suitable PAK recipients with type 1 diabetes who received a deceased kidney transplant, does PAK transplant increase life expectancy or improve quality of life?
B.5 In suitable PAK recipients with type 2 diabetes, does PAK transplant increase life expectancy or improve quality of life?
B.6 In suitable PAK recipients with type 2 diabetes, does PAK transplant after a live kidney donor transplant increase life expectancy or improve quality of life?
B.7 In suitable PAK recipients with type 2 diabetes, does PAK transplant after deceased donor kidney transplant increase life expectancy or improve quality of life?
C. Impact of pancreas transplantation alone (PTA)
C.1 In suitable recipients, is PTA associated with increased risk of death when compared to current medical therapies?
C.2 In suitable PTA recipients, is PTA associated with increased risk of earlier renal failure compared to current medical therapy?
C.3 In suitable PTA recipients, does PTA extend longevity or improve quality of life compared to current medical therapies?
C.4 After the first post-transplant year, is PTA superior to current medical therapies for metabolic control?
C.5 Is PTA superior to current medical therapies in the course of chronic complications of diabetes?
C.6 Is PTA superior to current medical therapies in the course of diabetic retinopathy?
C.7 Is PTA superior to current medical therapies in the course of diabetic nephropathy?
C.8 Is PTA superior to current medical therapies in the course of diabetic neuropathy?
C.9 Is PTA superior to current medical therapies in the course of cardiovascular disease?

was encouraged to suggest changes and also to add relevant questions that were possibly missed by the steering committee. After the final approval of questions, expert groups began their work in January 2019.

The following experts participated in online Delphi rounds but were not present in Pisa at the consensus conference for audience voting: Peter J. Friend, Osama A. Gaber, Takashi Kenmochi, Paolo Rigotti, Antonio Secchi, Robert J. Stratta, and Christopher C.E. Watson.

TABLE 3 Questions on technical issues

1. Activity volume and innovation in pancreas transplantation
1.1 What is the minimally acceptable annual volume of pancreas transplants per center?
1.2 What is the minimally acceptable annual volume of pancreas transplants per surgeon?
1.3 Is there a role for segmental live donor pancreas transplantation in non-immunized recipients?
1.4 Is there a role for segmental live donor pancreas transplantation in immunized recipients?
1.5 What are the anticipated risks for the live donor?
1.6 Is there evidence that minimally invasive pancreas transplantation increases the risk of the transplant procedure versus open pancreas transplantation?
1.7 Is there evidence that minimally invasive pancreas transplantation is associated with worse long-term results versus open pancreas transplantation?
1.8 Is there evidence of benefits from minimally invasive pancreas transplantation?
1.9 Is there evidence that minimally invasive pancreas transplantation is more beneficial in obese versus lean pancreas transplant recipients?
2. Pancreas donation
2.1 In the setting of DBD, is age >40 years an absolute or relative contraindication to pancreas transplantation?
2.2 In the setting of DBD, is the use of pediatric donors an absolute or relative contraindication to pancreas transplantation?
2.3 In the setting of DBD, is donor BMI >30 kg/m^2 a contraindication to pancreas transplantation?
2.4 Is DCD an absolute or relative contraindication to pancreas transplantation?
2.5 Is the University of Wisconsin solution superior to Celsior solution for pancreas preservation?
2.6 Is the University of Wisconsin solution superior to HTK solution for pancreas preservation?
2.7 Is the University of Wisconsin solution superior to IGL–1 solution for pancreas preservation?
2.8 Are quick en bloc techniques superior to conventional techniques for pancreas procurement?
2.9 Is the outcome of local versus imported grafts superior in pancreas transplantation?
2.10 For how long can pancreas grafts be ideally preserved?
2.11 Is machine perfusion of pancreas allografts feasible and associated with improved pancreas transplant outcomes?
3. Pancreas graft allocation
3.1 In SPK transplants, are the results of AB0-identical/-compatible transplantation superior to those of AB0-incompatible transplantation?
3.2 In solitary pancreas transplants, are the results of AB0-identical/-compatible transplantation superior to those of AB0-incompatible transplantation?
3.3 In SPK transplants, are the results of cross-match negative transplants superior to those of cross-match positive transplants?
3.4 In solitary pancreas transplants, are the results of cross-match negative transplants superior to those of cross-match positive transplants?
3.5 In SPK transplants, in the setting of negative crossmatch, are the results of transplantation affected by the presence of DSA with MFI levels <3000?
3.6 In SPK transplants, in the setting of negative crossmatch, are the results of transplantation affected by the presence of DSA with MFI levels <5000?
3.7 In solitary pancreas transplants, in the setting of negative crossmatch, are the results of transplantation affected by the presence of DSA with MFI levels <3000?
3.8 In solitary pancreas transplants, in the setting of negative crossmatch, are the results of transplantation affected by the presence of DSA with MFI levels <5000?
3.9 In SPK transplants, are the results of transplantation improved by reduced HLA mismatching?
3.10 In solitary pancreas transplants, are the results of transplantation improved by reduced HLA mismatching?
3.11 Should kidneys be preferentially allocated to SPK recipients, when compared to recipients of kidney alone transplants?
3.12 Should kidneys be preferentially allocated to SPK recipients, when compared to recipients of kidney alone transplants with a PRA ≥80%?
3.13 Should kidneys be preferentially allocated to SPK recipients, when compared to recipients of other simultaneous transplants (i.e., liver-kidney, heart-kidney, and lung-kidney)?
3.14 Are the results of SPK transplants in type 1 diabetic patients superior to the results of SPK transplants in type 2 diabetic patients so that a priority should be given to type 1 diabetics?
3.15 Are the results of SPK transplants in patients aged ≤50 years superior to the results of SPK in older patients so that a priority should be given to younger recipients?
4. Recipient selection for pancreas transplantation (SPK, PAK, and PTA)
4.1 Is there a higher risk of posttransplant renal failure in potential PTA recipients with normal (eGFR ≥90 ml/min/1.73 m^2) or mildly decreased (eGFR 60–89 ml/min/1.73 m^2) renal function and nephrotic syndrome when compared to recipients without nephrotic syndrome?
4.2 Is there a higher risk of posttransplant renal failure in potential PTA recipients with normal (eGFR ≥90 ml/min/1.73 m^2) or mildly decreased (eGFR 60–89 ml/min/1.73 m^2) renal function and proteinuria (without nephrotic syndrome) when compared to recipients without proteinuria?
4.3 Does PTA improve the course of chronic diabetic complications as compared to state of the art medical therapies?
4.4 Are the results of PAK transplants performed in recipients with a creatinine clearance ≤45 ml/min inferior to the results of PAK transplants performed in patients with higher creatinine clearance or eGFR levels?
4.5 Are the results of PAK transplants performed in recipients with history of renal rejection inferior to the results of PAK transplants performed in patients without an history of renal rejection?
4.6 Are the results of PAK transplants performed within 6 months from renal transplantation inferior to the results of PAK transplants performed after this time interval?
4.7 Are the results of preemptive SPK transplants superior to those of SPK transplants performed in patients undergoing dialysis?
4.8 Are the results of SPK transplants in obese patients inferior when compared to the results of SPK transplants in non-obese patients?
4.9 Are the results of SPK transplants in patients with lower limb amputation inferior to the results of SPK transplants in patients without an history of lower limb amputation?
4.10 Are the results of SPK transplants in patients with an history of coronary heart disease inferior to the results of SPK transplants in patients without an history of coronary heart disease?

(Continues)

TABLE 3 (Continued)

5. Surgical techniques for pancreas transplantation
5.1 Is pancreas transplantation with bladder drainage associated with more frequent surgical complications when compared to pancreas transplantation with enteric drainage?
5.2 Is pancreas transplantation with bladder drainage associated with more frequent urologic and metabolic complications when compared to pancreas transplantation with enteric drainage?
5.3 Is SPK transplants with bladder drainage associated with superior immunologic outcomes when compared to SPK transplants with enteric drainage?
5.4 Is solitary pancreas transplants with bladder drainage associated with superior immunologic outcomes when compared to pancreas transplants with enteric drainage?
5.5 Is pancreas transplantation with portal venous drainage associated with higher rates of surgical complications when compared to pancreas transplantation with systemic venous drainage?
5.6 Is pancreas transplantation with portal venous drainage superior to pancreas transplantation with systemic venous drainage, with respect to immunologic outcome?
5.7 Is pancreas transplantation with portal venous drainage superior to pancreas transplantation with systemic venous drainage, with respect to metabolic parameters?
5.8 Is duodeno-duodenal anastomosis associated with more frequent surgical complications when compared to duodeno-jejunal anastomosis?
5.9 Is duodeno-duodenal anastomosis associated with improved immunologic outcome when compared to duodeno-jejunal anastomosis?
5.10 Is intraperitoneal pancreas placement associated with more frequent surgical complications when compared to retroperitoneal pancreas placement?
5.11 Is graft accessibility for percutaneous biopsy improved by retroperitoneal versus intraperitoneal pancreas graft placement?
6. Immunosuppression in pancreas transplantation
6.1 Is steroid usage versus steroid avoidance associated with improved immunologic outcomes?
6.2 Is steroid usage versus early steroid withdrawal associated with improved immunologic outcomes?
6.3 Is steroid avoidance versus steroid usage associated with improved metabolic parameters?
6.4 Is early steroid withdrawal versus steroid maintenance associated with improved metabolic parameters?
6.5 Is induction versus no induction therapy associated with improved immunologic outcomes?
6.6 Is induction versus no induction therapy associated with more early complications?
6.7 Is induction versus no induction therapy associated with more oncologic complications?
6.8 Is induction therapy with depleting antibodies versus induction therapy with non-depleting antibodies associated with improved immunologic outcomes?
6.9 Is induction therapy with depleting antibodies versus induction therapy with non-depleting antibodies associated with more early complications?
6.10 Is induction therapy with depleting antibodies versus induction therapy with non-depleting antibodies associated with more oncologic complications?
6.11 Is CNI-free immunosuppression associated with inferior immunologic outcomes in pancreas transplantation when compared to CNI-including immunosuppression?
6.12 Is CNI-free immunosuppression associated with reduced toxicity in pancreas transplantation when compared to CNI-including immunosuppression?
6.13 Is tacrolimus superior to cyclosporine, with respect to immunologic outcomes, in SPK transplants?
6.14 Is tacrolimus superior to cyclosporine, with respect to immunologic outcomes, in solitary pancreas transplants?
6.15 Is once-a-day tacrolimus formulation superior to twice-a-day tacrolimus formulation in pancreas transplantation?
6.16 Is the use of mycophenolate formulations versus aziathioprine associated with improved immunologic outcomes in pancreas transplantation?
6.17 Is the use of mycophenolate formulations versus aziathioprine associated with more side effects in pancreas transplantation?
6.18 Is the use of m-TOR inhibitors versus mycophenolate formulations associated with improved immunologic outcomes in pancreas transplantation?
6.19 Is the use of mycophenolate formulations versus m-TOR inhibitors associated with more side effects in pancreas transplantation?
6.20 Is m-TOR-based immunosuppression versus CNI-based immunosuppression associated with improved immunologic outcomes in pancreas transplantation?
6.21 Is m-TOR-based immunosuppression versus CNI-based immunosuppression associated with more side effects in pancreas transplantation?
6.22 Is m-TOR-based immunosuppression versus CNI-based immunosuppression associated with increased formation of DSA in pancreas transplantation?
6.23 Is delayed introduction of m-TOR inhibitors better tolerated than immediate m-TOR-inhibitors introduction in pancreas transplantation?
7. Post-operative prophylaxis in pancreas transplantation
7.1 Does antithrombotic prophylaxis versus no prophylaxis reduce the rate of pancreas graft thrombosis in SPK transplants?
7.2 Does antithrombotic prophylaxis versus no prophylaxis reduce the rate of pancreas graft thrombosis in solitary pancreas transplantations?
7.3 Does antithrombotic prophylaxis versus no prophylaxis reduce the rate of deep venous thrombosis and pulmonary embolism in SPK transplants?
7.4 Does antithrombotic prophylaxis versus no prophylaxis reduce the rate of deep venous thrombosis and pulmonary embolism in solitary pancreas transplantations?
7.5 Is anticoagulation superior to anti-aggregation/antiplatelet therapy in antithrombotic prophylaxis to prevent pancreas graft thrombosis in pancreas transplant recipients?
7.6 Does antiviral prophylaxis versus no prophylaxis reduce the incidence of CMV infection in pancreas transplant recipients?
7.7 Is antiviral prophylaxis superior to preemptive therapy in reducing the rate of CMV infection in pancreas transplant recipients?
7.8 Does antimycotic prophylaxis versus no prophylaxis reduce the rate of fungal infections in pancreas transplant recipients?
7.9 Does antimicrobial prophylaxis versus no prophylaxis reduce the rate of bacterial infections in pancreas transplant recipients?
7.10 Does vaccination versus no vaccination reduce the rate of infections in pancreas transplant recipients?

(Continues)

TABLE 3 (Continued)

8. Immunology in pancreas transplantation
8.1 Does surveillance evaluation of DSA levels improve the immunologic outcome of pancreas transplantation versus no surveillance serology?
8.2 Does surveillance pancreas biopsy improve the immunologic outcome of pancreas transplantation versus no surveillance biopsy in SPK transplants?
8.3 Does surveillance pancreas biopsy improve the immunologic outcome of pancreas transplantation versus no surveillance biopsy in solitary pancreas transplants?
8.4 In SPK transplants, is a first rejection episode best treated with steroid pulses or T cell-depleting antibodies?
8.5 In solitary pancreas transplant recipients, is a first rejection episode best treated with steroid pulses or T cell-depleting antibodies?
8.6 In SPK transplants, is a second rejection episode best treated with steroid pulses or T cell-depleting antibodies?
8.7 In solitary pancreas transplant recipients, is a second rejection episode best treated with steroid pulses or T cell-depleting antibodies?
8.8 What is the ideal treatment of antibody-mediated rejection in SPK transplants?
8.9 What is the ideal treatment of antibody-mediated rejection in solitary pancreas transplantation?
8.10 Autoimmune recurrence. How patients should be surveilled?
9. Follow-up after pancreas transplantation
9.1 What are the effects of SPK transplant on retinopathy?
9.2 What are the effects of SPK transplant on development/occurrence of diabetic nephropathy in the kidney graft?
9.3 What are the effects of SPK transplant on neuropathy?
9.4 What are the effects of SPK transplant on the cardiovascular system?
9.5 What are the effects of SPK transplant on quality of life?
9.6 What are the effects of PTA on retinopathy?
9.7 What are the effects of PTA on nephropathy?
9.8 What are the effects of PTA on neuropathy?
9.9 What are the effects of PTA on the cardiovascular system?
9.10 What are the effects of PTA on quality of life?

Abbreviations: BMI, body mass index; CNI, calcineurin inhibitors; CMV, cytomegalovirus; DBD, donation after brainstem death; DSA, donor specific antibodies; eGFR, estimated glomerular filtration rate; HLA, human leukocyte antigens; HTK, histidine-tryptophan-ketoglutarate; IGL-1, institute Georges Lopez -1; MFI, mean fluorescent intensity; PAK, pancreas after kidney transplant; PRA, panel reactive antibody; PTA, pancreas transplant alone; SPK, simultaneous pancreas and kidney.

TABLE 4 Zurich–Danish model for independent consensus

	Organizing committee	Expert panels	Jury
Phase 1—Preparation	• Determines the topics • Selects the expert panels• Selects the jury	• Draft evidence-based document for each topic• Propose recommendations	• Revises the manuscripts submitted by the experts
Phase 2—Conference meeting	• Chairs the presentations• Ensures the discussion	• Present the evidence • Propose the recommendations • Discuss with the jury and the audience • Revise recommendations if appropriate	• Asks questions to the experts• Asks the vote of the audience on the recommendations
Phase 3—Deliberations			• Produces the final recommendations

3.3 | Online Delphi rounds

Two online Delphi rounds were run among expert groups for all questions.

3.4 | On-site discussions and live voting

The consensus meeting was held on two consecutive days (October 18 and 19, 2019) and was organized in sessions matching the predefined topics. Before each voting session, experts from working groups were asked to give presentations covering the questions to be addressed. After discussion of presentations, a summary of results of systematic literature review was also presented. Next, suggested recommendations were presented for audience discussion and vote (agreement rate ≥85%). Up to three voting rounds were allowed for each recommendation. Proportion of agreement was recorded for each question.

3.5 | Definitions

Sensitization (or sensitized patient) was defined as the presence of circulating antibodies directed against human leukocyte antigens.[17] High sensitization (or highly sensitized patients) was defined as a panel reactive antibody >85%.[18]

Obesity was defined according to World Health Organization (i.e., body mass index ≥30 kg/m^2).[19] Obesity classes (i.e., classes I–III), as well as ethnicity variations affecting obesity definition, were not considered because of lack of granular data in available literature.

TABLE 5 Quality of evidence in GRADE

A. High quality of evidence	Consistent evidence from well-performed randomized, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk.
B. Moderate quality of evidence	Evidence from randomized, controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other form. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate.
C. Low quality of evidence	Evidence from observational studies, unsystematic clinical experience, or from randomized, controlled trials with serious flaws. Any estimate of effect is uncertain.

Abbreviation: GRADE, grading of recommendations, assessment, development, and evaluations.

TABLE 6 GRADE recommendations

Quality of evidence	Strong recommendation	Weak recommendation
High quality of evidence	1A Benefits clearly outweigh risk and burdens, or vice versa.	2A Benefits closely balanced with risks and burdens.
Moderate quality of evidence	1B Benefits clearly outweigh risk and burdens, or vice versa.	2B Benefits closely balanced with risks and burdens, some uncertainty in the estimates of benefits, risks, and burdens.
Low quality of evidence	1C Benefits appear to outweigh risk and burdens, or vice versa.	2C Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens.

Abbreviation: GRADE, grading of recommendations, assessment, development, and evaluations.

Preemptive SPK transplantation was defined as the combined transplantation of a pancreas and a kidney in patients with stage 4/5 chronic kidney disease before they initiate dialysis.

4 | OVERALL RESULTS OF SYSTEMATIC LITERATURE REVIEWS

Results of systematic literature reviews are provided in Figure 2. Overall, 52 488 papers met the inclusion criteria in the 12 searches.

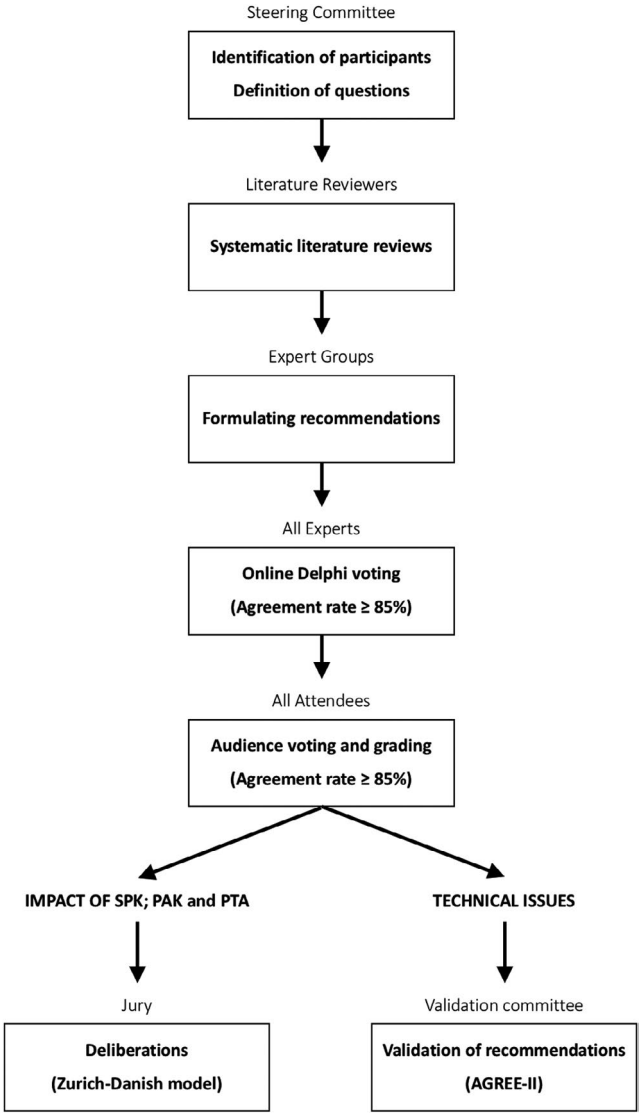

FIGURE 1 Flow chart of guideline process

After removal of duplications (−5341) and application of exclusion criteria (−42 399), and following review of titles and abstracts (−4151), 597 studies were included in summaries for guideline production.

5 | RESULTS OF SYSTEMATIC LITERATURE REVIEWS FOR IMPACT OF PANCREAS TRANSPLANTATION ON THE CARE OF DIABETES

5.1 | Impact of SPK

Literature search was finalized on July 20, 2019, using the terms "(simult*) and (pancr*) and (kidn* or ren*) and (transpl*)", revealing 1879 articles. After removal of duplication and application of exclusion criteria (−1306), and following review of titles and abstracts (−542), 31 studies were included in summaries for guideline production (Appendix 1).

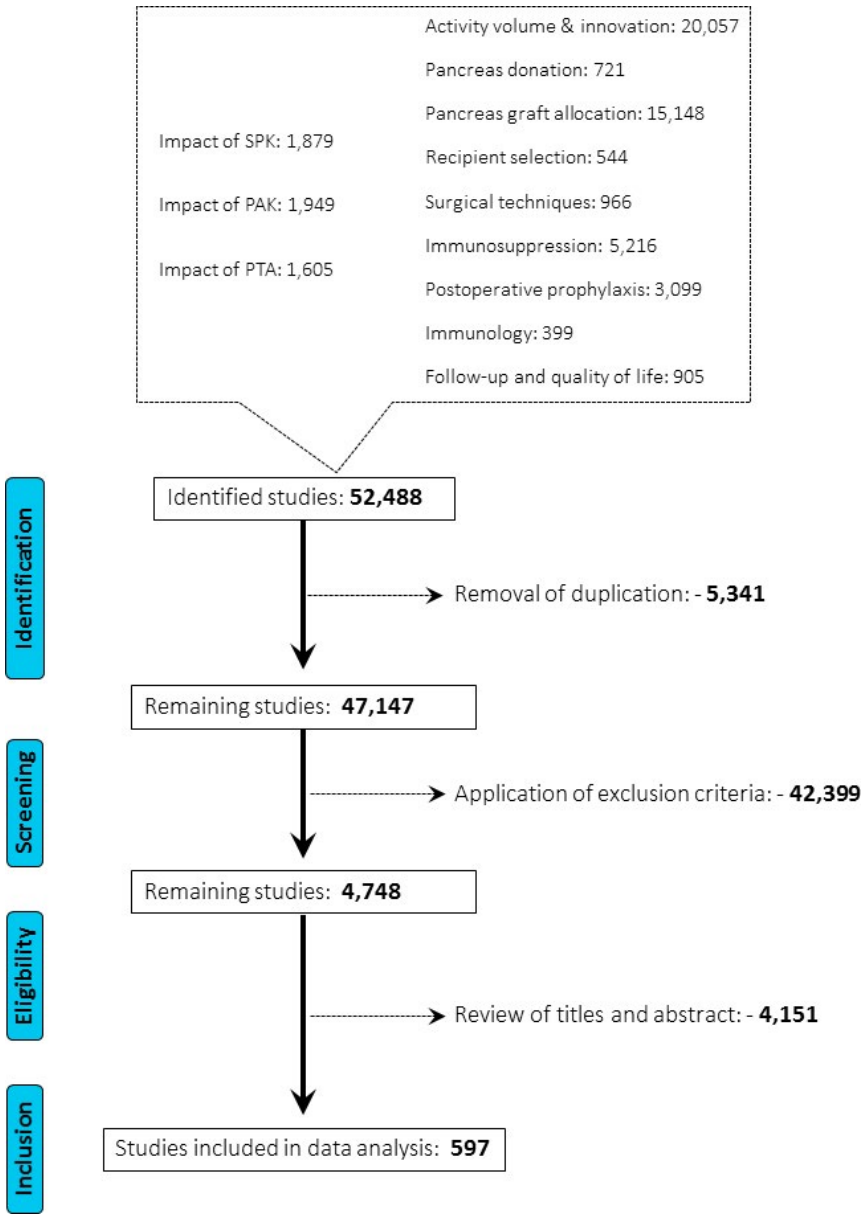

FIGURE 2 Flow chart of literature reviews

5.2 | Impact of PAK

Literature search was finalized on September 9, 2019, using the terms (pancr*) and (trans*) and (after) and (kidney) and (diabetes). A total of 1949 articles were identified. After removal of duplications and application of exclusion criteria (−1,877), and following review of titles and abstracts (−39), 33 studies were included in summaries for guideline production (Appendix 1).

5.3 | Impact of PTA

Literature search was finalized on September 9, 2019, using the terms "pancrea*" (All Fields) and "transplan*" (All Fields) and ("alone" [All Fields] OR "solitary" [All Fields]), revealing 1605 articles. After removal of duplications and application of exclusion criteria (−1386), and following review of titles and abstracts (−180), 39 studies were included in summaries for guideline production (Appendix 1).

6 | RESULTS OF SYSTEMATIC LITERATURE REVIEWS FOR TECHNICAL ISSUES RELATED TO THE PRACTICE OF PANCREAS TRANSPLANTATION

6.1 | Activity volume and innovation in pancreas transplantation

Literature search was finalized on October 1, 2019, using the terms (pancr*) and (transpl*), revealing 20 057 articles. After removal of duplications and application of exclusion criteria (−19 547), and following review of titles and abstracts (−480), 30 studies were included in summaries for guideline production (Appendix 1).

6.2 | Pancreas donation

Literature search was finalized on October 1, 2019, using the terms "(pancr*) and (donation)", revealing 721 articles. After removal of duplications and application of exclusion criteria (−463), and following review of titles and abstracts (−196), 62 studies were included in summaries for guideline production (Appendix 1).

6.3 | Pancreas graft allocation

Literature search was finalized on August 5, 2019, using the terms (pancr*) and (organ*) and (transpl*), not (cancer*) not (tumor*) not (carcin*) not (neopla*), in order to include all the papers that could address pancreas transplantation but also other solid organ transplants, aiming to identify also those reports discussing allocation policies for other organs or for specific categories of recipients. A total of 15 148 articles were identified. After removal of duplications and application of exclusion criteria (−14 781), and following review of titles and abstracts (−336), 31 studies were included in summaries for guideline production (Appendix 1).

6.4 | Recipient selection for pancreas transplantation (SPK, PAK, and PTA)

Literature search was finalized on September 10, 2019, using the terms "(pancr*) and (transpl) and (recipient) and (selection)", revealing 544 articles. After removal of duplications and application of exclusion criteria (−432), and following review of titles and abstracts (−63), 49 studies were included in summaries for guideline production (Appendix 1).

6.5 | Surgical techniques for pancreas transplantation

Literature search was finalized on July 20, 2019, using the terms (transpl*) and (pancr*) and (portal* OR system*) and (bladd* OR enter*) and (duoden* OR digiun*), revealing 966 articles. After removal of duplications and application of exclusion criteria (−466), and following review of titles and abstracts (−444), 56 studies were included in summaries for guideline production (Appendix 1).

6.6 | Immunosuppression in pancreas transplantation

Literature search was finalized on July 22, 2019, using the terms (pancr*) and (transpl*) and (immunosupp*), revealing 5216 articles. After removal of duplications and application of exclusion criteria (−3412), and following review of titles and abstracts (−1657), 147 studies were included in summaries for guideline production (Appendix 1).

6.7 | Post-operative prophylaxis in pancreas transplantation

Literature search was finalized on August 12, 2019, using the terms (pancr*) and (transplant*) and (prop*), revealing 3099 articles. After removal of duplications and application of exclusion criteria (−2720), and following review of titles and abstracts (−340), 39 studies were included in summaries for guideline production. Specifically, 12 articles were identified regarding antimycotic prophylaxis, 8 regarding antimicrobial prophylaxis, 9 regarding antiviral prophylaxis, and 9 regarding antithrombotic prophylaxis. Two articles reported consensus guidelines on the management of cytomegalovirus and vaccination in solid organ transplants, respectively. One article reported on both antimycotic and antiviral prophylaxis (Appendix 1).

6.8 | Immunology in pancreas transplantation

Literature search was finalized on August 26, 2019, using the terms ("pancreas transplantation" [Majr]) and ("graft rejection" [Majr] or "protocol biopsy" or "donor specific antibodies" or "DSA" or "autoimmune recurrence" or "autoimmunity" or "diabetes recurrence"), revealing 399 articles. After removal of duplications and application of exclusion criteria (−293), and following review of titles and abstracts (−70), 36 studies were included in summaries for guideline production (Appendix 1).

6.9 | Follow-up after pancreas transplantation

Two different literature reviews (on diabetic complications and quality of life) were performed to address follow-up. Both searches were finalized on July 31, 2019.

The literature review on diabetic complications using the terms ("pancreas transplantation") and ("diabetic retinopathy" or "diabetic neuropathy" or "diabetic nephropathy" or "cardiovascular") revealed 543 articles. After removal of duplications and application of exclusion criteria (−291), and following review of titles and abstracts (−221), 31 studies were included in summaries for guideline production (Appendix 1).

The literature review on quality of life using the terms ("pancreas transplantation") and ("quality of life") revealed 362 articles. After removal of duplications and application of exclusion criteria (−173), and following review of titles and abstracts (−176), 13 studies were included in summaries for guideline production (Appendix 1).

7 | DISCUSSION

In the first 50+ years of pancreas transplantation,[1] with more than 50 000 cases reported to the International Pancreas Transplant Registry,[20] and probably several hundred unreported cases performed worldwide, there has been no occasion in which the international community had convened to reach a consensus on either the impact of

pancreas transplantation on the care of patients with diabetes or the technical issues concerning the practice of this procedure. Previous actions[4-6] have indeed focused on very specific issues, while covering the full spectrum of therapeutic options for β cell replacement.

In 2014, IPITA organized a scientific workshop in Oxford, England, in collaboration with the Transplantation Society, to review the status and research agenda of β cell replacement therapies. Topics of this workshop included whole organ pancreas transplantation, isolated islet transplantation, artificial pancreas, immunological tolerance, xenotransplantation, encapsulation technologies, β cell regeneration, and stem cell-derived β cells. This scientific workshop was not organized in the format of a consensus conference but did produce a summary for each of the eight selected topics, not presented in the form of recommendations.[4]

In 2017, IPITA organized a 2-day workshop in Igls, Austria, in collaboration with the European Pancreas and Islet Transplant Association. Declared aims of the workshop were to develop consensus for an IPITA/European Pancreas and Islet Transplant Association statement on the definition of function and failure of current and future forms of β cell replacement therapies; to review the metabolic and immunologic outcome measures used to select patients and assess the efficacy of β cell replacement therapies and guide therapeutic decisions; to ensure consistency of definitions for glycemic control metrics within the field of artificial pancreas device development; and to build a network of collaborators to foster scientific synergy in the clinical investigation of various β cell replacement and artificial insulin delivery approaches to diabetes. Although consensus criteria for the definition of β cell replacement therapy functional outcomes and success ("the Igls criteria") were produced and published, this meeting was indeed a workshop, rather than a formal consensus conference.[5,6]

The present conference was specifically designed to provide evidence-based recommendations for the practice of pancreas transplantation using specific, standardized, and validated methods. We also decided, for the first time ever, to define the impact of the main types of pancreas transplantation in the management of patients with diabetes. Information from this part of the consensus could be used for key decisions such as prioritization of patients for graft allocation (within the diabetic population and with respect to other recipient populations competing for the same grafts), acceptance of transplant risks (as compared with continued medical management), assessment of risk/benefit balance at the time of transplantation in the context of donor quality, and additional risk factors (such risk of transmission of infection or cancer). To avoid any conflict of interest, deliberations on these issues were made by an independent jury according to the Zurich–Danish model.[11]

Although the range of application of artificial pancreas[21,22] and other forms of β cell replacement[23] may have some overlap with pancreas transplantation, we specifically decided to limit our consensus conference to pancreas transplantation given the extent of knowledge to be reviewed and assessed.

For the impact of pancreas transplantation in the management of patients with diabetes, we identified 35 questions (SPK, 19; PAK, 7; and PTA, 9). For the technical issues, we identified 109 questions that were categorized into nine main topics. After several online Delphi rounds[16] and exhaustive audience discussions and votings, recommendations were approved by a group of experts and eventually validated by an additional and independent group of experts using the AGREE II instrument.[8] Quality of evidence was assessed using the SIGN methodology,[9] and each recommendation was graded,[10] thus providing evidence-based guidelines for the practice of pancreas transplantation.

Another key feature of our consensus conference is that we did not receive any funding or support from any commercial company. The successful organization of a conference free of any potential commercial bias was made possible by a 2-year fundraising effort to secure financial support from local institutions, mostly based on the commitment of local members of the steering committee. The degree of difficulty involved in bias-free fundraising may have been among the reasons why this type of a consensus conference had never been held in the past.

Overall, over 52 000 publications were identified, leading to the definition of 597 full-text articles to be included in the quantitative analysis (Appendix 1). There were few prospective and randomized studies, mostly relating to immunosuppression. In contrast to most other areas of medicine, pancreas transplantation is not particularly suitable for prospective and randomized studies, considering that most institutions are low volume, that procedures are performed non-electively, and that patients with diabetes requiring a pancreas transplant are extremely complex. Additionally, for many years, the main questions in pancreas transplantation related to solving practical issues, such as surgical technique, preservation injury, and immunological graft failure, with proportionally less time devoted to well-designed clinical studies. Having said that, as a pancreas transplant community, we should probably acknowledge that for too many years we have been more committed "to do" rather than to rigorously study pancreas transplantation and provide high levels of evidence. Now that the number of pancreas transplants is decreasing worldwide,[24] to design and conduct such studies would be even more complex. However, we should move into this direction, by collaborative efforts, and provide the missing pieces of evidence. Only these types of studies could better motivate our colleagues from medical disciplines to refer more patients for pancreas transplantation before the evolution of chronic complications of diabetes that can influence outcomes of the procedure or render it futile.

Review of 50+ years of literature and extraction of data from several hundreds of articles was truly a major undertaking that could have intrinsic limitations and carry the risk of unintentional selection bias. Despite the creation of several dedicated teams for literature review, sharing and presentation of results of literature search, and online and in-person discussion of each statement, we acknowledge that some articles could have been missed. Additionally, Ovid/Medline was not included in the systematic reviews. Finally, only data from full peer-reviewed manuscripts were considered, thus potentially missing data from abstracts that could have provided additional information.

In conclusion, we have presented the methods and the results of literature search used for the First World Consensus Conference on

Pancreas Transplantation. Results of the consensus conference are presented in detail in a separate manuscript in this issue of the journal.

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DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding authors upon request.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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APPENDIX A

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(Continues)

APPENDIX A (Continued)

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