Value of renography in kidney transplantation

BELNUC Virtual Seminar – Update on kidney and bladder imaging



Stan Benjamens, MD, PhD



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- Young Professionals in Transplantation board
 - European Society for Organ Transplantation





PhD-thesis: Medical Imaging before and after kidney transplantation





- 1. History of transplantation and imaging
- 2. Trends in current transplantation
- 3. Need for imaging research
- 4. Renography studies
- 5. Future advancements (PET and MRI)



Kidney transplantation

- Saints Cosmas and Damian
- The miracle of the transplantation of the black leg
- Jaume Huguet, 15th century





Kidney transplantation

- First successful kidney transplantation
- Dog-to-dog transplant five days of function
- Emerich Ullmann in Vienna, Austria, 1902



Kidney transplantation

- First available diagnostic image
- X-ray after pyelosil contrast
- Dempster, 1950



1. Dempster, Ann R Coll Surg Engl. 1950



Renography

- Introduction of radiotracers in 1960s
- First Iodine-131-Hippuran renogram 1965
- Replaced by Technetium-99m mercaptoacetyltriglycine (MAG3) in 1988



2. Collins and Wilson, Ann Surg. 1965



Trends in kidney transplantation

- Dutch trends
- Increase in deceased donor age





Trends in kidney transplantation

- Increase in recipient age
- High prevalence of cardiovascular risk factors





Need for imaging research

- Bibliometric study on
 - Imaging research
 - Transplantation research
 - Past 21-years
- Transplantation guidelines



3. Benjamens, Eur Rad, 2018



Need for imaging research

- 5.6% of transplant publications focused on imaging
- Imaging publications 1 14.8% yearly
- Transplant publications 1 2.3% yearly



3. Benjamens, Eur Rad, 2018



Tracers

- MAG3 most used, high plasma protein binding capacity (90%)
- DTPA direct measurement of glomerular filtration, lower imaging quality



3. Benjamens, Transpl Reviews, 2018



Indications

- Urologic complications:
 - Urine leakage and obstruction
- Fluid collections:
 - Lymphocele
 - Urinoma
 - Hematoma
- Vascular complications:
 - Stenosis
 - Thrombosis



3. Benjamens, Transpl Reviews, 2018



Complications after kidney transplantation

	Complication	Incidence (%)	
Renal complications			
	Acute rejection (AR)	8% - 10% 47,48	
	Acute tubular necrosis (ATN)	22% ⁴⁹	
Vascular complications			
	Transplant renal artery stenosis (TRAS)	1 - 23% ^{35,36}	
	Transplant renal artery thrombosis (TRAT)	0.8% - 3% ^{35,37}	
	Transplant renal vein thrombosis (TRVT)	1.0% - 1.8% ^{35,37}	
Urological complications			
	Urinary tract obstruction	4.5 - 4.7 ^{42,43}	
	Urinary leak	1.5 - 1.6 ^{42,43}	
Postoperative fluid collections			
	Urinoma	a	
	Hematoma	4.9% ⁵⁰	
	Abscess	0.3% 51	
	Lymphocele	5.2% ⁵²	
^a no data available			

3. Benjamens, Transpl Reviews, 2018



- Visual interpretation
 - MAG3 SPECT imaging: showing urine leak at 1 day after renal transplantation and resolved leak at 4 days after transplantation.



3. Benjamens, Transpl Reviews, 2018



- Qualitative assessment of tracer uptake and perfusion
- Heaf and Iversen grading scale



Benjamens, Transpl Reviews, 2018
Heaf and Iversen, Eur J Nucl Med, 2000



• Quantitative assessment



Benjamens, Transpl Reviews, 2018
Yazici, Clin Nuc Med, 2016



- Delayed graft function (DGF)
 - Need for dialysis in 1st seven days after transplantation
 - Serum creatinine decrease <10% after transplantation
- Prolonged hospitalisation
- Increased risk of graft loss
- Higher post-transplant mortality

6. Benjamens, PLOS One, 2018



- Prognostic performance for duration of DGF
- 2000 2014, dual centre study (Groningen and Leiden)
- 377 patients
- MAG3 Renography within 3-days after transplantation

6. Benjamens, PLOS One, 2018



• 4 grade qualitative assessment



6. Benjamens, PLOS One, 2018



- Four quantitative indices:
 - tubular function slope (TFS)
 - corrected tubular extraction rate (cTER)
 - Average slope
 - R20/3





6. Benjamens, PLOS One, 2018



 Qualitative and quantitative analysis for ≥ 7 days delayed graft function

Index		Cut-off	Sensitivity, %	Specificity, %	PPV, %	NPV, %	AUC
Qualitative							
	RS Grade	>2	87	65	87	65	-
Quantitative							
	TFS	0.64	80	61	84	53	0.75
	cTER	262	76	72	88	52	0.80
	MUC10	825	64	77	88	44	0.75
	Average upslope	0.47	75	73	88	52	0.82

6. Benjamens, PLOS One, 2018



- High sensitivity
- Low specificity

6. Benjamens, PLOS One, 2018



- Need for dialysis and length of hospital stay
- 2011 to 2014, Leiden
- 200 first and 108 consecutive procedures
- MAG3 renography within 3 and 7 days

7. Benjamens, Eur Rad, 2020



- Qualitative assessment
 - First renography
 - Second renography
 - And combined data



7. Benjamens, Eur Rad, 2020



 Duration of delayed graft function and length of hospital stay based on qualitative grading

			Duration of DGF		Length of hospital stay	
		Patients, n	Median	IQR	Median	IQR
First scintigraphy						
	Grade 1 and 2	30	5.0	2.0 - 7.0	11.0	12.0 - 19.0
	Grade 3	89	7.0	6.3 - 10.0	15.0	12.0 - 19.0
	Grade 4	41	11.0	7.5 - 19.5	20.0	14.0 - 28.5
Second scintigraphy						
	Grade 2	25	7.0	7.0 – 7.5	14.0	12.0 - 16.5
	Grade 3	52	8.0	7.0 - 10.0	15.0	12.3 - 19.0
	Grade 4	31	15.0	10.0 - 20.0	22.0	15.8 - 29.3

7. Benjamens, Eur Rad, 2020



- Single renography:
 - Reliable indication for DGF duration and length of hospital stay
- Low additional value of consecutive procedure

7. Benjamens, Eur Rad, 2020



- Focusing on replacing renal biopsies for the diagnosis of rejection
- & pre-transplant viability assessment

7. Benjamens, Eur Rad, 2020



- Rat-model for kidney transplant rejection
- Sample of 21, with 3 cases of rejection
- FDG uptake correlates with inflammation
- Sensitivity 98.8%
- Specificity 92.0%



8. Reuter S, PLoS ONE 2009



- Post-transplant prove of concept
- 32 patients, 8 cases of rejection
- FDG correlates with BNAFF rejection score
- Sensitivity 100%
- Specificity 50%

BK nephropathy Acute rejection Borderline Normal Acute rejection Borderline Representation Borderline Representatio Borderline Representation Borderline

CT

PET

PET/CT

9. Lovinfosse P, Am J Transplant. 2016



- Prospective study
- Discriminating rejection from other complications or normal function
- 79 patients, 23 cases of rejection
- Area under the curve 0.86
- Sensitivity 100%
- Specificity 30%

9. Lovinfosse, J Nuc Med Mol Imaging, 2021





- Shortage of organ donors
- Use of suboptimal donors
- Need for viability testing



10. Schutter, Art Organs, 2022



- MRI-ASL/T2-weighted imaging
- Increase in cortical perfusion during three hours of perfusion



10. Schutter, Art Organs, 2022



- MRI-Diffusion Tensor Imaging (DTI)
- 54 patients, 11 worsening function
- Correlation between DTI and function



11. Wen-jun Fan, Eur Rad 2016





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