

4TH GCC KIDNEY TRANSPLANTATION & NEPHROLOGY CONGRESS

Follow-up Of Kidney Transplant Recipients In 2025: Towards An Individualized Approach

Mohamed Mongi BACHA

- Professor of Nephrology, Department of Internal Medicine “A”, Charles Nicolle Hospital and Faculty of Medicine of Tunis
- Vice-President of the Tunisian Society of Nephrology, Dialysis and Kidney Transplantation (STNDT)
 - Expert at the National Center for the Promotion of Organ Transplantation (CNPTO), Tunisia
 - Organization Committee Chair of the 18th AFRAN Congress, April 15-18, 2025, Tunis, Tunisia
 - Chair of the African Association of Nephrology (AFRAN) Transplant Committee

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AFRAN 2025 CONGRESS

Tunis, Tunisia - April 15 - 18, 2025
Raddison Blu Hotel & Convention Center
(Ex. Laico Hotel)

18th

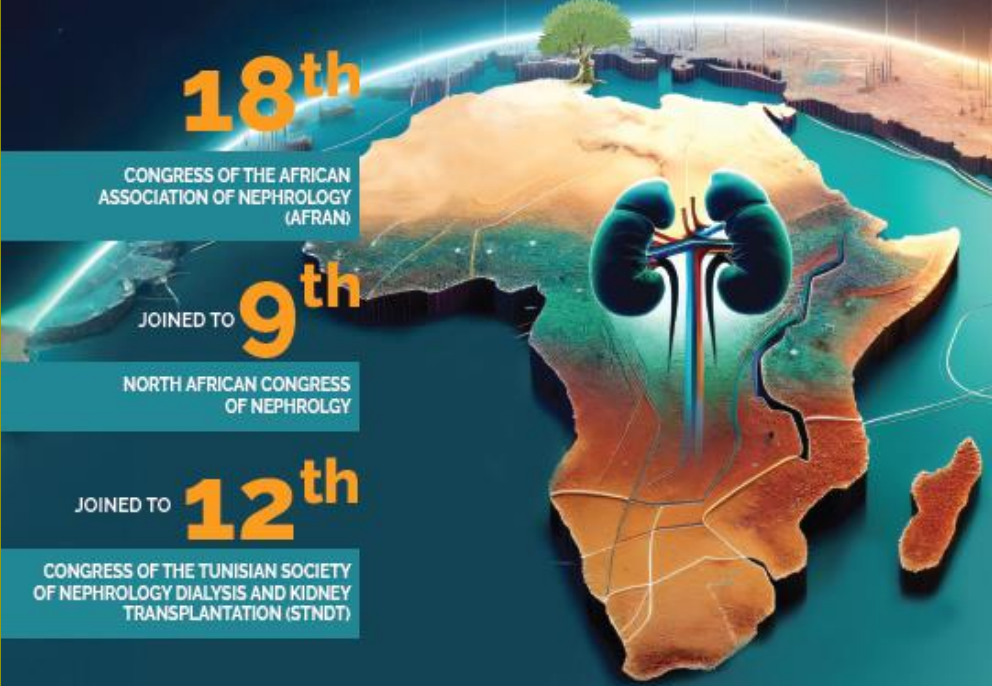
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INTRODUCTION

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■ **Post-Kidney Transplant Follow-up :**

- ✓ Long, complex and costly process
- ✓ Key to good graft and patient survival
- ✓ Must be extremely rigorous
- ✓ Enables prevention and early management of complications
- ✓ Well codified, depends on the post-transplant period : short (first weeks), medium (3 to 12 months) and long term (> 1year)
- ✓ Facilitated by new communication technologies

OBJECTIVES

A- In The Short Term :

- 1- Prevent acute rejection
- 2- Optimize graft function
- 3- Prevent infections

B- In The Medium And Long Term :

- 1- Preserve good graft function
- 2- Ensure good therapeutic adherence
- 3- Prevent the consequences of immunosuppression : metabolic, infectious, neoplastic, cardiovascular, etc.

RECOMMANDATIONS (I)



HAUTE AUTORITÉ DE SANTÉ

SYNTHESE DES RECOMMANDATIONS PROFESSIONNELLES

Suivi ambulatoire de l'adulte transplanté rénal au-delà de 3 mois après transplantation

Novembre 2007

<https://www.has-sante.fr/>

RECOMMENDATIONS (2)



RECOMMENDATIONS (3)

ARAB JOURNAL OF UROLOGY
2021, VOL. 19, NO. 2, 105–122
<https://doi.org/10.1080/2090598X.2020.1868657>



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RENAL TRANSPLANTATION: REVIEW ARTICLE

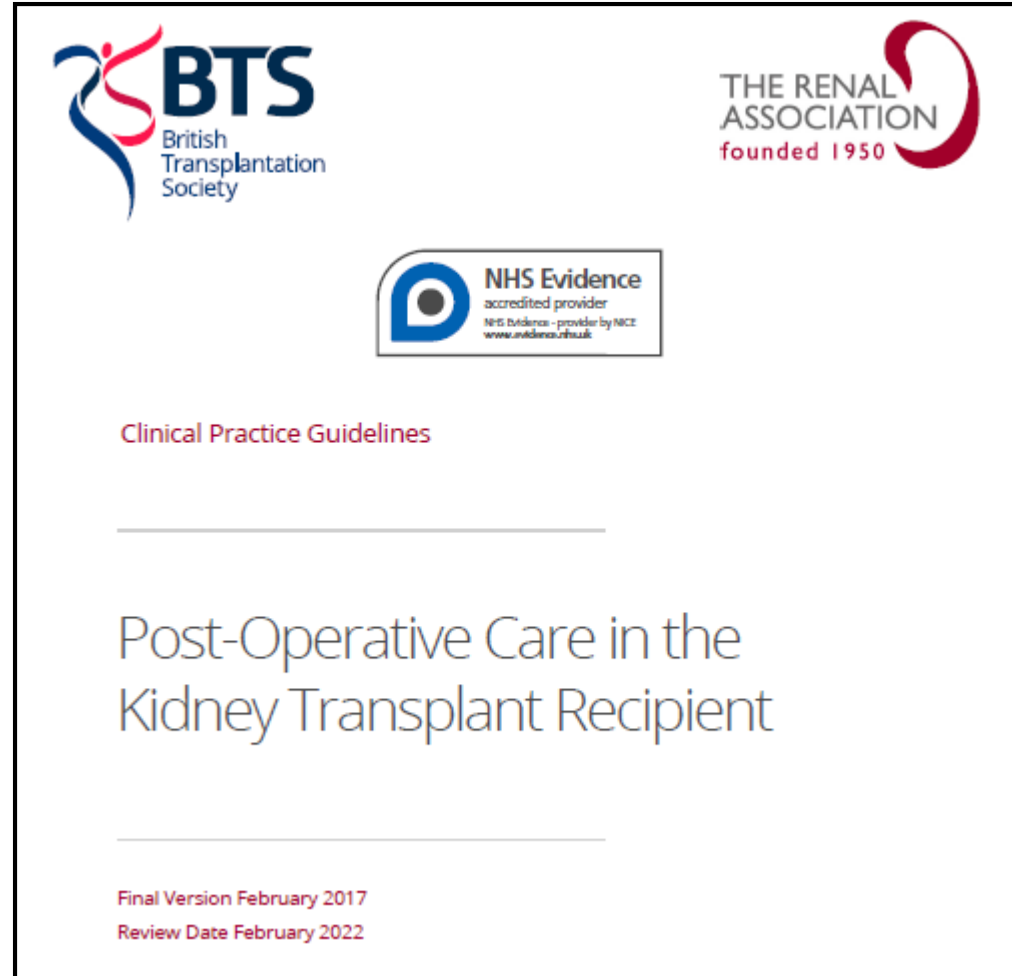
 OPEN ACCESS

 Check for updates

Egyptian clinical practice guideline for kidney transplantation

Shokeir A. Arab J Urol 2021;19(2)2:105-22.

RECOMMENDATIONS (4)



<https://ukkidney.org/sites/renal.org/files/FINAL-Post-Operative-Care-Guideline-1.pdf>

RECOMMENDATIONS (5)



Wettstein D. Langenbecks Arch Surg 2014;399(4):415-20.



Mamode N. Transplant Int 2022;35:10511.

OUTLINE

I- GENERAL FOLLOW-UP ORGANIZATION

- 1-** NECESSARY INFRASTRUCTURE
- 2-** LOCATION AND ACTORS
- 3-** RHYTHMICITY OF CONSULTATIONS
- 4-** CALENDAR
- 5-** DATA TO BE TRANSMITTED BY THE TRANSPLANT CENTER
- 6-** CONTACT AND/OR PATIENT TRANSFER TO THE TRANSPLANT CENTER
- 7-** TELE-CONSULTATION SOLUTION

II- KIDNEY ALLOGRAFT FOLLOW-UP

- 1-** RENAL FUNCTION MONITORING
 - A-** GFR ESTIMATE
 - B-** GFR MEASURE
- 2-** ANATOMICAL MONITORING
- 3-** HISTOLOGICAL MONITORING
- 4-** BIOMARKERS

III- IMMUNOLOGICAL MONITORING

IV- MONITORING OF IMMUNOSUPPRESSION AND ITS COMPLICATIONS

- 1-** PHARMACOLOGICAL MONITORING
- 2-** THERAPEUTIC ADHERENCE MONITORING
- 3-** PREVENTION AND SCREENING OF COMPLICATIONS
 - A-** METABOLIC : NODAT
 - B-** INFECTIOUS : BK VIRUS NEPHROPATHY
 - C-** NEOPLASTIC : CANCERS AND PTLD

I- GENERAL FOLLOW-UP ORGANIZATION

1- NECESSARY INFRASTRUCTURE

NECESSARY INFRASTRUCTURE

Guideline 1.1 – KTR: Clinic infrastructure

We suggest that the following infrastructure should be in place for KTR follow up (2D):

- A consultant-level health care professional should be available for every transplant clinic
- KTRs should be reviewed in a dedicated outpatient area
- The results of blood tests (including drug levels if possible) should be available within 24 hours
- A formal mechanism should exist for results review by health care professionals within 24 hours of a clinic appointment
- There should be access to a multidisciplinary renal team including pharmacist, dietician, social worker and psychologist
- Patient care should be planned along principles set out in the National Service Framework and “Kidney Health Delivering Excellence”

2- LOCATION AND ACTORS

- **Follow-up Location :**

- ✓ **First months :**

- In the transplant center

- ✓ **Subsequent monitoring (beyond three months) :**

- Organized by the transplant center

- **Actors : Shared (alternating) monitoring between :**

- ✓ Transplant center physicians

- ✓ Physicians likely to be involved in subsequent outpatient follow-up
(Referring Nephrologist, Cardiologist, General Practitioner, etc.)

3- RHYTHMICITY OF CONSULTATIONS

RHYTHMICITY OF CONSULTATIONS

Guideline 1.2 – KTR: Clinic frequency

We suggest that uncomplicated patients may be reviewed progressively less frequently (2C)

- 2-3 times weekly for the first month after transplantation
- 1-2 times weekly for months 2-3
- Every 2-4 weeks for months 4-6
- Every 4-6 weeks for months 6-12
- 3-6 monthly thereafter



Box 29: Annual review

- We suggest that every transplant centre establishes a multispecialty annual review clinic for the appraisal of its KTRs at their KT anniversaries

4- CALENDAR

Suivi	4 à 6 mois	7 à 12 mois	Au-delà de 1 an
Examen clinique / Anamnèse	1 x / 2 semaines		
Ionogramme sanguin : Na, K, Cl, HCO ₃ ⁻ , protides	1 x / 2 semaines		
Bilan hépatique : ALAT, ASAT, gamma-GT	1 x / 2 semaines		
Surveillance de la fonction rénale et du transplant			
- Créatinémie et estimation du débit de filtration glomérulaire	1 x / 2 semaines		
- Protéinurie des 24 heures ou rapport protéinurie/créatininurie	1 x / 2 semaines		
- Bandelette urinaire, et ECBU si bandelette positive	1 x / 2 semaines		
- Ponction-biopsie rénale	En cas d'altération d'apparition		
Suivi immunologique			
- Recherche d'anticorps anti-HLA (classes I et II)	1 x / an et l'immunosupp		
Surveillance des immunosuppresseurs			
- Effets indésirables des immunosuppresseurs	1 x / 2 semaines		
- Suivi pharmacologique :			
- Immunosuppresseurs à index thérapeutique étroit (ciclosporine, tacrolimus, sirolimus, évérolimus) : concentration sanguine	1 x / 2 semaines		
- Pour tout immunosuppresseur : concentration sanguine ou plasmatique	En cas ou de risque		
- Observance thérapeutique	1 x / 2 semaines		
Prévention du risque cardio-vasculaire			
- Pression artérielle	1 x / 2 semaines		
- Anomalies glucidiques : glycémie (à jeun)	1 x / 2 semaines		
- Anomalies lipidiques : bilan lipidique			
- Obésité : indice de masse corporelle (IMC)	1 x / 2 semaines		
- Suivi cardiologique (ECG, échocardiographie)			
- Homocystéinémie			
- Fistule artério-veineuse : surveillance de la fonction ventriculaire par échocardiographie	1 x / an en cas d		
Suivi de la polyglobulie ou de l'anémie			
- Hémogramme	1 x / 2 semaines		
Autres suivis biologiques			
- Urémie			
- Magnésémie	En cas de symptô		
Suivi carcinologique			
- Lymphomes :			
- Chez les patients à risque : signes cliniques	Au moins		
- Chez les patients EBV séronégatifs receveurs d'un transplant EBV séropositif : réplication virale par PCR	Au moins 1 x / 3 signes d		
- Cancers cutanés : examen cutanéomuqueux complet :			
- Chez tous les patients	Avant la transplantation, sinon dans les 6 mois après		
Suivi	4 à 6 mois	7 à 12 mois	Au-delà de 1 an
- En cas d'antécédent de carcinome spinocellulaire ou de kératoacanthome			
- En présence d'autres lésions pré-malignes ou malignes			
- Biopsie de lésion verruqueuse cutanée ou muqueuse			
- Cancers urologiques :			
- Tumeur rénale ou urothéliale : échographie du haut et bas appareil urinaire, tomodensitométrie, cystoscopie si examens précédents négatifs			
- Tumeur rénale : échographie des reins natifs			
- Cancers des autres organes solides (prostate, oïdon, seins, col de l'utérus)			
Suivi osseux			
- Ostéopénie et ostéoporose :			
- Mesure de la taille			
- Interrogatoire : recherche des facteurs de risque de fracture			
- Calcémie et phosphatémie	1 x / 2 sem		
- Dosage sérique de vitamine 25(OH)D3 et parathormone	À 3 mo		
- Examen densitométrique osseux	Avant la t normal, l'ex sinon, ou		
- Ostéonécrose : IRM du bassin			
Suivi infectieux			
- Infection et maladie à cytomégalovirus (CMV) :			
- Réplication virale	En cas de d'organe, l		
- Statut sérologique du patient et réplication virale	En fonction		
- Infection à parvovirus B19			
- Infection à papillomavirus : examen cutanéomuqueux			
- Infection à herpes virus humain 8 (HHV8) : examen cutanéomuqueux à la recherche d'une maladie de Kaposi chez les patients transplantés HHV8 séropositif			
- Infections à virus Herpes simplex (HSV) et virus varicelle zona (VZV) : traitement et prophylaxie idem population générale, sauf :			
- En cas de lésion extensive ou de localisation méningée d'une infection à HSV ou VZV	Trait		
- Pour les patients transplantés séronégatifs pour le VZV et potentiellement à risque d'un contage	Prop		
- Pneumocystose : prophylaxie	Prophylaxie adéquat		
- Toxoplasmose	Diagnostic symptom		
- Infection à BK virus (BKV) : recherche dans le sang ; si test positif : à confirmer dans les 4 semaines et/ou suivi d'un test quantitatif dans le sang	- Dépistage années post		
	- En cas de lésions évocatrices sur biopsie rénale		
Suivi	4 à 6 mois	7 à 12 mois	Au-delà de 1 an
- Hépatite B (VHB) :			
- Dosage plasmatique des anticorps anti-HBs	1 x / 3 mois		
- Recherche des marqueurs de cirrhose ou de carcinome hépatocellulaire			
- Hépatite C (VHC) : recherche d'une évolution vers une cirrhose ou un cancer, ainsi que les signes d'atteinte rénale et systémique liée au VHC			
- Infection par le VIH :			
- Recherche d'infection ano-génitale à papillomavirus			
- Tuberculose :			
- Radiographie du thorax			
- Test tuberculinique cutané, ou intradermoréaction à la tuberculine (IDR)			
- Bilan hépatique			
- Infections à pneumocoque			
- Vaccinations			
Suivi urologique et chirurgical			
- Bandelette urinaire, et ECBU si bandelette positive	1 x / 2 semaines	1 x / mois	1 x / 1 à 4 mois
- Recherche d'un obstacle de la voie urinaire ou d'une tumeur du transplant : échographie du transplant		1 x / an	
- Recherche d'une sténose de l'artère rénale ou d'une obstruction de la voie urinaire : échographie Doppler du transplant			En cas de dégradation de la fonction rénale ou d'apparition d'une hypertension artérielle
- Recherche d'un reflux vésico-urétéral			En présence de pyélonéphrites aiguës récidivantes
Suivi de la fonction sexuelle			
- Évaluation et prise en charge adaptées			À la demande du patient
Contraception et grossesse			
- Contraception :			
- Contraception progestative			La plus souvent proposée
- Contraception œstroprogestative			Peut être utilisée (mais rechercher systématiquement les facteurs de risque thromboembolique artériel et veineux)
- Dispositifs intra-utérins			Généralement contre-indiqués
- Grossesse : information et prise en charge adaptée			Suivi obstétrical effectué en collaboration avec le médecin en charge du suivi de la transplantation
Suivi de la qualité de vie			
			Éducation thérapeutique avec suivi multidisciplinaire

(Les examens surlignés sont pratiqués lors de chaque consultation du suivi systématique)

5- DATA TO BE TRANSMITTED BY THE TRANSPLANT CENTER

Critère n°1. Transmission des données en vue du suivi partagé

Recommandation source

Au début du suivi partagé, il est recommandé que le centre de transplantation transmette au médecin correspondant (néphrologue, médecin traitant, etc.) les éléments détaillés dans le tableau 1 [des recommandations] :

- les antécédents du patient, en particulier néphrologiques ;
- les caractéristiques de la transplantation ;
- les données du suivi des 3 premiers mois ;
- les éléments cliniques et biologiques post-transplantation au moment du début du suivi partagé ;
- les modalités de suivi du patient, les traitements en cours, et avant tout le type et les modalités d'immunosuppression ;
- les coordonnées des personnes à contacter dans le centre de transplantation.

DATA TO BE TRANSMITTED (2)

Patient medical history, particularly nephrological	- Initial nephropathy - Dialysis duration and type - Previous transplantation
Characteristics of transplantation	- Donor type: living; brain dead - Donor's age - HLA incompatibility and prior immunization - Donor and recipient serological status (HBV, HCV, CMV and EBV) - Cold and warm ischemia times
Three-month post-transplant follow-up data	- Surgical report - Initial hospitalization report - Reports of any rehospitalizations - Follow-up reports from the 1st to the 3rd post-KT months
Patient's post-transplant clinical and biological data at the start of shared follow-up	- Last creatinine level and its lowest value - Last eGFR - Last uroculture, proteinuria assay and proteinuria/creatinuria ratio - Last lipid profile (total cholesterol, HDL, LDL, TG) - Last US of the transplant - Pre- and post-transplant bone densitometry if available

DATA TO BE TRANSMITTED (3)

Type and modalities of immunosuppression and other ongoing treatments	- Immunosuppression protocol and therapeutic ranges - Associated treatments - Expected changes in immunosuppression and other treatments (dosages envisaged and planned dates)
Follow-up modalities	- Dates of any scheduled interventions - Consultation dates scheduled in the transplant center - Therapeutic education program
Contact details at the transplant center	- Contact details of referring physicians - Emergency contact details

OUR STANDARD REPORT

UNITE

Nom	:	
Prénom	:	
Date de naissance	:	01/01/1954
Nationalité	:	Sénégalaise
Statut social	:	Marié, 5 enfants
Dossier N°	:	48114
Hospitalisation	:	Du 14/03/2012 à
Motif d'hospitalisation	:	Transplantation
Couverture sociale	:	Payant
Profession	:	Commerçant

Patient hypertendu connu depuis 2000 avec une l'association de plusieurs antihypertenseurs. Une insuffisance rénale chronique, secondaire très vasculaire hypertensive, a été diagnostiquée en 2010. Le stade terminal a été retenu en Août 2011.

Un traitement de suppléance par hémodialyse péritonéale a été mis en place au Centre de dialyse de Dakar (Sénégal) à l'Association ASSOFAAL, à raison d'une séance hebdomadaire.

Son abord vasculaire est un cathéter jugulaire droit artérioveineux radiale gauche a été confectionné et rapidement thrombosée.

Son poids sec est de 75 kg, sa prise de poids diurèse résiduelle est d'environ 250 ml/jour.

Au cours de la période de dialyse, Monsieur MAMA présente :

- Une hyperparathyroïdisme secondaire, non traité.
- Une anémie nécessitant un traitement par érythropoïétine (HEMA® à la dose de 400 U/kg/sem) et transfusé.
- Son Hb était à 12,9 g/dl en début de traitement.

- Groupe sanguin : O (+) Positif.
- Phénotype : C Négatif, c Positif, E Négatif, e Positif, Kell N
- Typage HLA: A₂-A₃₄ ; B₃₅-B₅₀ ; DR₀₃-DR₀₇
- Recherche d'anticorps cytotoxiques : négative

- **Echographie abdomino-pelvienne** : reins diminués de kyste polaire inférieur du rein droit de 3,3 cm de diamètre prostate homogène augmentée de taille de poids estimé à 37 g.
- **Urétro-cystographie rétrograde** : surélévation de la vésical. Rétrecissement régulier de l'urètre prostatique (évident prostatique). Absence de reflux vésico-urétéral actif ou passif vésical post-mictionnel.
- **L'examen urologique**, réalisé par le Pr Chebil au service Charles Nicolle de Tunis, note une prostate de consistance non 20 gr. Au vu de cet examen, des données biologiques (PSA des données de l'imagerie, il n'y avait pas de contre-indication rénale et le patient sera mis sous alpha bloquer prostatique).
- **Echographie cardiaque trans-thoracique** : cardiomegaly concentrique avec fonction systolique globale et segment d'éjection du ventricule gauche à 62%), insuffisance aortique.
- **Echo-doppler des tronc vasculaires supra-aortiques** : infiltrées avec présence de plaques bilatérales non sténosantes.
- **Echographie doppler des membres inférieurs** : sans.
- **Fibroscopie oeso-gastro-duodénale** : normale.
- **Examen ophtalmologique** : acuité visuelle à 10/10 (hors rétinopathie hypertensive chronique stade 3, de choroïdopathie chronique et de neuropathie ischémique hypertensive gauche). antitransfèrent plaquettaire est souhaitable afin de prévenir rétinienne.
- **Examen Oto-Rhino-Laryngologique** : rhinite purulente favorable après antibiotérapie.
- **Examen stomatologique** : plusieurs caries dentaires. Intraire.
- **Examen parasitologique des selles** : présence de Histolytica et de Blastocystis Hominis. Un traitement par métrastauré instauré avec un contrôle parasitologique des selles négatif.
- **Coproculture** : négative.
- **Sérologies** :

HVC	HIV	CMV	EBV	HSV
Négative	Négative	IgG = 32 IgM négative	IgG positive IgM négative	IgG = 64 IgM négative

- HVB : Ag HBs positif, Ac anti-HBe positif, Ac anti-HBc de type IgM négatif.
La recherche d'ADN du virus de l'hépatite B quantitative, était négative.
- La sérologie de la leishmaniose est négative.

Monsieur [REDACTED] âgé de 31 ans, est le fils du [REDACTED]
antécédent un asthme au jeune âge.

- A l'examen physique : sa pression artérielle est de 120/29,3 kg/m² et l'examen des urines à la bandelette réactive est négatif.
- A la biologie : sa créatininémie est à 110 µmol/l, sa glycémie à jeun à 1,16 mmol/l et la microalbuminurie est à 166 mg/l.
- L'échographie rénale montre 2 reins de taille normale.
- L'angio-scanner rénal objective 1 artère à droite et 2 artères à gauche.
- Groupe sanguin : O (+) Positif.
- Typage HLA : A₂₃A₂₄C₄ ; B₃₅B₃₃ ; DR₀₁DR₁₀.
- Cross Match : négatif.
- Sérologies : négatives.

Aq Hbs	HVC	HIV	CMV	EBV	HSV
négatif	Négative	négative	IgG positive IgM négative	IgG positive IgM négative	IgG positif IgM négatif

La transplantation rénale a été réalisée le 15/03/2012 par le Urologue de l'Hôpital Charles Nicolle de Tunis. Le rein perçait une artère et une veine. Il a été transplanté dans la fosse iliaque vasculaire termino-latérale sur les vaisseaux iliaques externes derrière l'artère iliaque externe. A noter que la veine iliaque a une paroi cartonnée, difficile à disséquer et qu'elle présente paroi dédoublée faisant craindre une dissection post-opératoire au déclapement. L'ischémie chaude était de 51 minutes. Analgésie Lich Grégoire sur une sonde JJ.

- **Le traitement immunosuppresseur** d'induction a (Méthylprednisolone) à la dose de 1 mg/kg/j, de l'ATG[®] lymphocytaire) à la dose de 100 mg/j pendant 7 jours et de Mofétil à la dose de 2 grammes/j.

- L'équorol® (Cyclosporine) a été introduit à 3 à la dose de 4
 - L'évolution en post greffe a été marquée par :
 - Une reprise immédiate de la diurèse avec une créatininémie jusqu'à 116 µmol/l à J26 post-greffe.
 - Ablation de la sonde JJ le 06/04/2012 sans incident.
 - Des troubles mictionnels importants à type de de pollakiurie (au catalogue mictionnel : plus de 40 mic/ml un volume par miction variable de 50 à 110 ml au entre 2 mictions consécutives variable de 13 à 75 min
- L'examen cytobactériologique des urines était négatif prostatique a montré une dilatation modérée des mesurant 15 mm, un pyélon avec une paroi épaisse, estimé à 87 ml en plus de l'hypertrophie prostatique.
- L'évolution des signes urinaires était progressivement l'introduction d'un alpha bloqueur prostatique (Mécip®)
- Un souffle à l'auscultation du greffon rénal, avec normale sans traitement. L'échographie doppler a normalement coloré, des résistances artérielles in

une franche accélération artérielle péri-anastomotique. La décision était l'abstention thérapeutique avec une surveillance clinique et échographique régulière.

- Il a été réhospitalisé au service le 17/04/2012. Il était apyrétique, sa pression artérielle était de 120/80 mm Hg, sa diurèse à 4,5 l/j et son poids à 73,5 kg. A la biologie, il avait une créatinémie à 134 µmol/l, une hémoglobine à 11,3 g/dl et une uroculture négative. La recherche de protéinurie était négative.
- **Son traitement de sortie associé :**
- Cortacyl® (Prednisone) 5 mg : 3 comprimés par jour (avec dégression progressive jusqu'à 2 comprimés par jour).
 - MMF® (Mycophénolate Mofétil) 500 mg : 2 comprimés, 2 fois par jour.
 - Equoral® (Cyclosporine) : 125 mg, 2 fois par jour.
 - Bactrim® (Triméthoprim-Sulfaméthoxazole) 400 mg : 1 comprimé par jour.
 - Mécir® (Tamsulosine Chlorhydrate) LP 0,4 mg : 1 comprimé par jour.
 - Ipproton® (Oméprazole) 20 mg : 1 gélule par jour.
 - Fumafer® (Fer) : 1 comprimé par jour.
 - Vitamine C® 500 mg : 1 comprimé par jour.
- Il sera suivi à la consultation du Professeur Taïeb BEN ARDAJ IAH.

Première transplantation rénale à partir d'un donneur vivant avec 5 mismatches HLA chez un homme âgé de 58 ans, Ag HBs positif, traité par hémodialyse depuis Août 2011 en raison d'une insuffisance rénale chronique terminale secondaire très probablement à une néphropathie vasculaire.

L'évolution post-greffe était favorable à part une dilatation modérée des cavités pyélo-calicelles et une franche accélération artérielle péri-anastomotique du greffon objectivées à l'échographie doppler. A surveiller.

Hanène EL KATEB
Résidente du Service

Dr Mohamed Mongi BACHA
Assistant Hospitalo-Universitaire
en Néphrologie

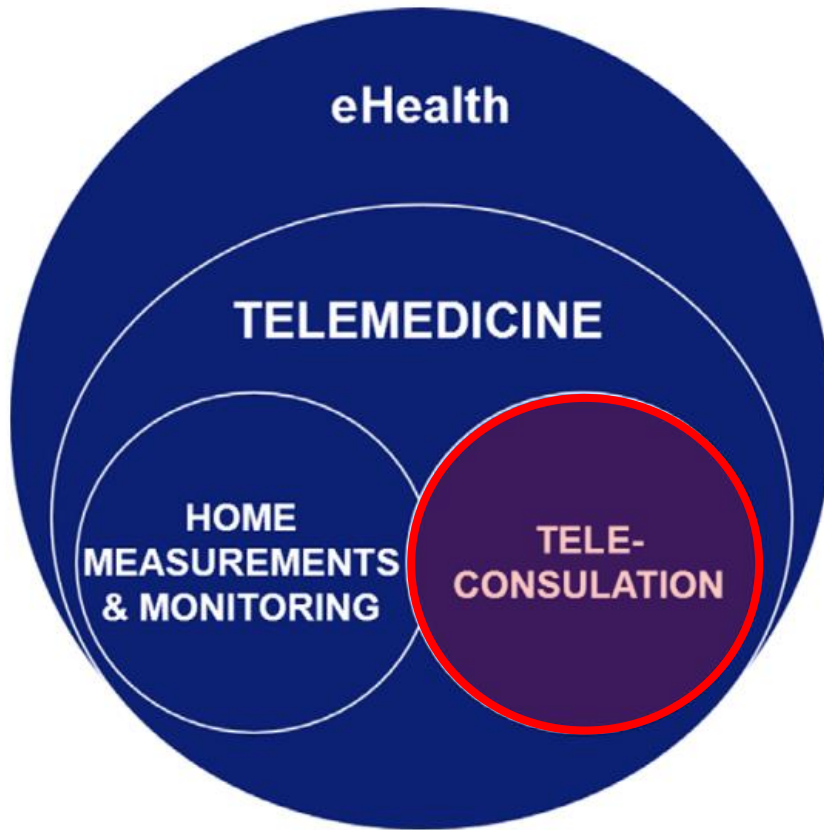
6- CONTACT AND/OR PATIENT TRANSFER TO THE TRANSPLANT CENTER

CONTACT AND/OR PATIENT TRANSFER TO THE TRANSPLANT CENTER

Signes cliniques	• Fièvre non expliquée par une pathologie infectieuse banale ou non rapidement résolutive (48-72 h) • Tension ou douleur du transplant • Hématurie macroscopique • Oligurie, anurie
Signes biologiques	• Élévation de la créatininémie ≥ 20 % par rapport à sa valeur la plus basse après transplantation • Anémie, leucopénie ou thrombopénie significatives • Augmentation significative de la protéinurie
Changements thérapeutiques	• Événement justifiant une modification majeure du traitement immunosuppresseur (vomissements empêchant la prise, suspicion d'événement indésirable grave...) • Reprise d'un traitement par épuration extrarénale ou proposition de réinscription en liste d'attente • Inclusion du patient dans un essai thérapeutique
Autres circonstances	• Patient non observant (traitement, consultations) • Indication d'une ponction-biopsie rénale • Hospitalisation quelle qu'en soit la cause • Projet de grossesse ou grossesse • Diabète • Toute pathologie sévère, notamment cancéreuse • Décès du patient

7- TELE-CONSULTATION SOLUTION

TELE-CONSULTATION



A healthcare service platform using **a live video consultation** that enables **real-time communication** between the patient and the provider **at a remote location**.

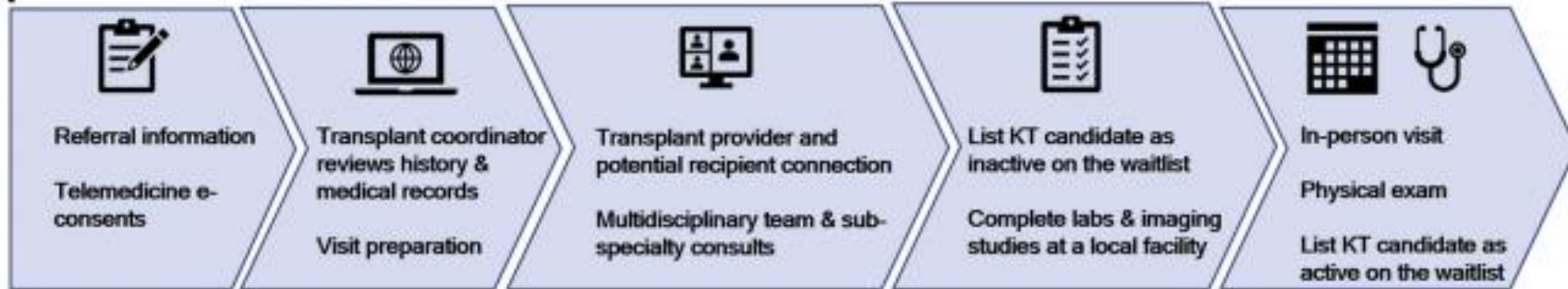
TELE-CONSULTATION AND KT :

BENEFITS

Benefit	Patient	Clinician	Hospital
Simplified logistics (reduced traveling)	✓		
Minimized risk of infection	✓	✓	✓
Quality of life	✓		
Potential reduction of the Clinician's burden and time optimization		✓	✓
Continuity of patient monitoring	✓	✓	✓
Efficient management of visit's processes (delegation, automation)		✓	
Use of innovative solutions for the optimal management and optimization of patient care			✓
Increased activity volumes (with the same resources)			✓
Formalization of informal clinician-patient interactions through GDPR compliant channels		✓	
Direct and indirect cost reductions (social costs)	✓		✓

TELE-CONSULTATION AND KT : INDICATIONS

A



B



C



TELE-CONSULTATION AND KT :

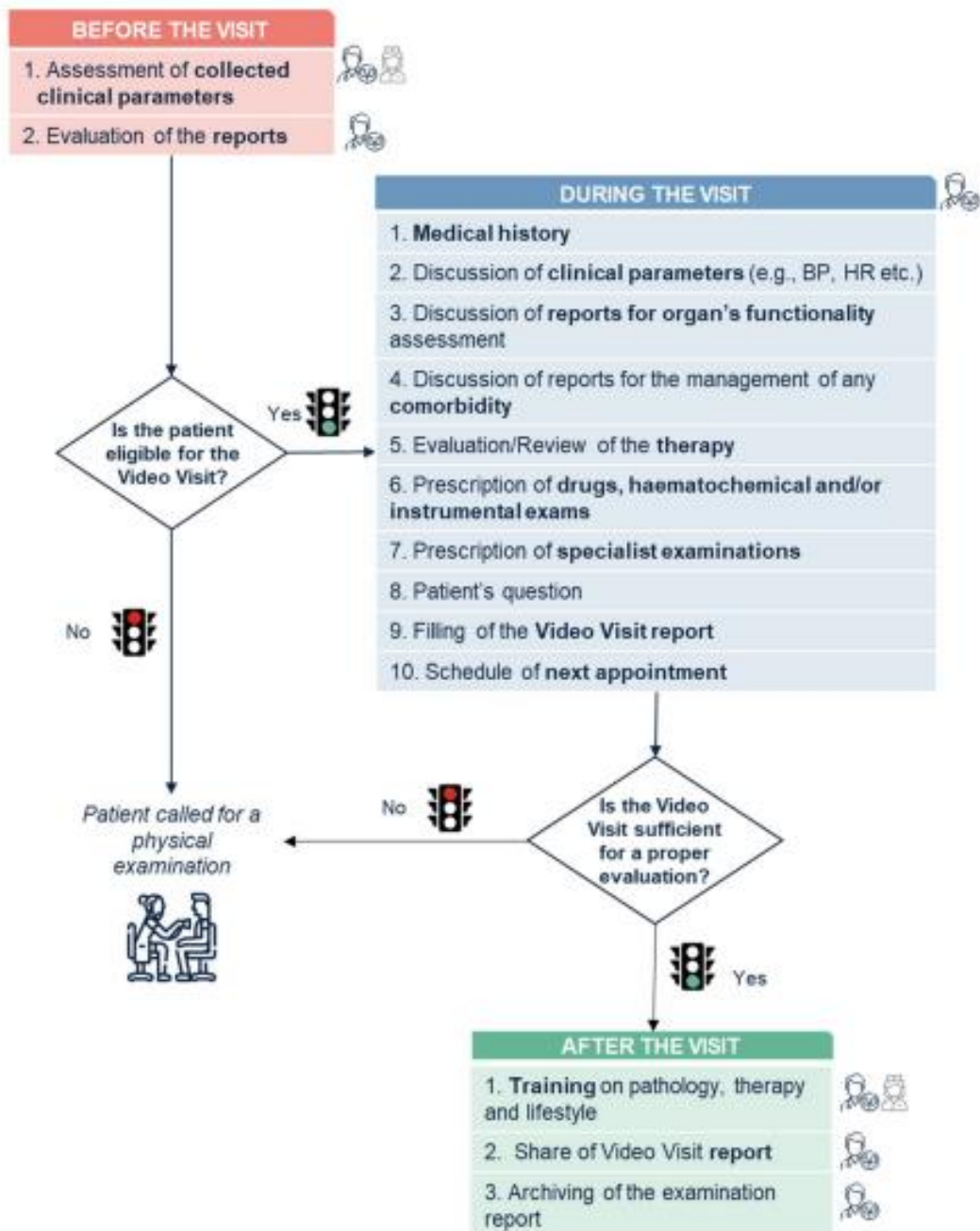
ELIGIBILITY CRITERIA

Patient characteristics and clinical status

- 18–70 years old
- Stable kidney function
- Established immunosuppressive therapy
- Low risk of comorbidities
- In the follow-up program for ≥ 12 months

Technical requirements

- Access to computer and/or mobile devices
 - Webcam
 - Audio and microphone
 - Absence of firewalls impeding the download and access to teleconference platforms
 - Good and stable Internet connection
 - Basic skills in the use of computer/mobile devices and apps for video calling
 - Presence of a caregiver for assistance if the above skills cannot be ensured
-



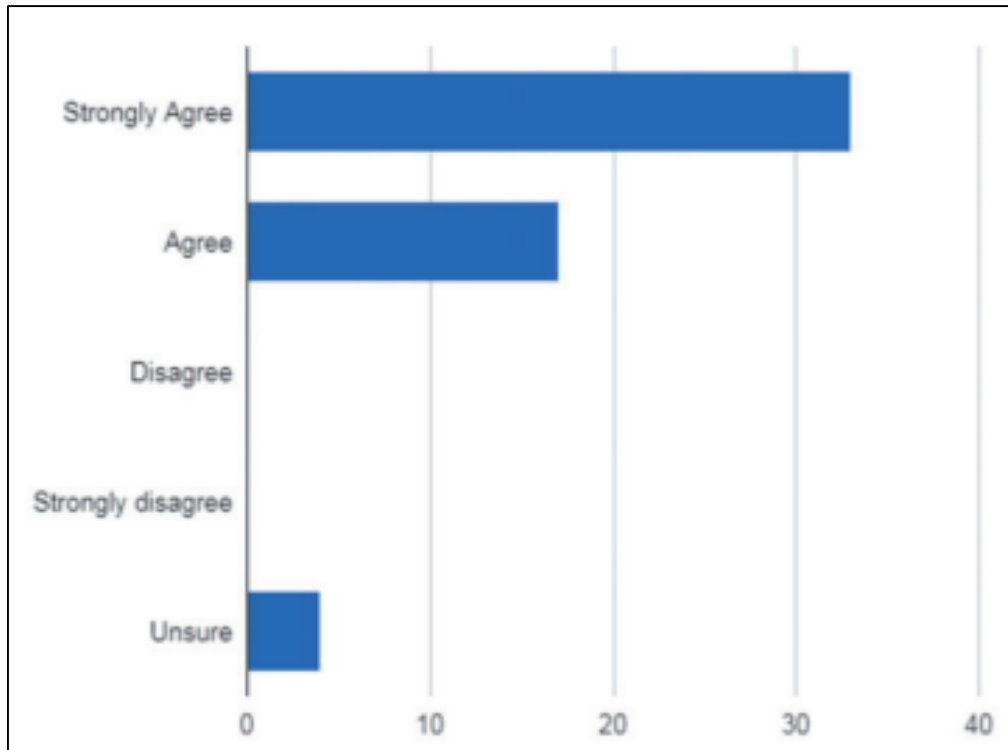
TELE-CONSULTATION AND KT : ORGANIZATION AND PROCEDURE

TELE-CONSULTATION AND KT :

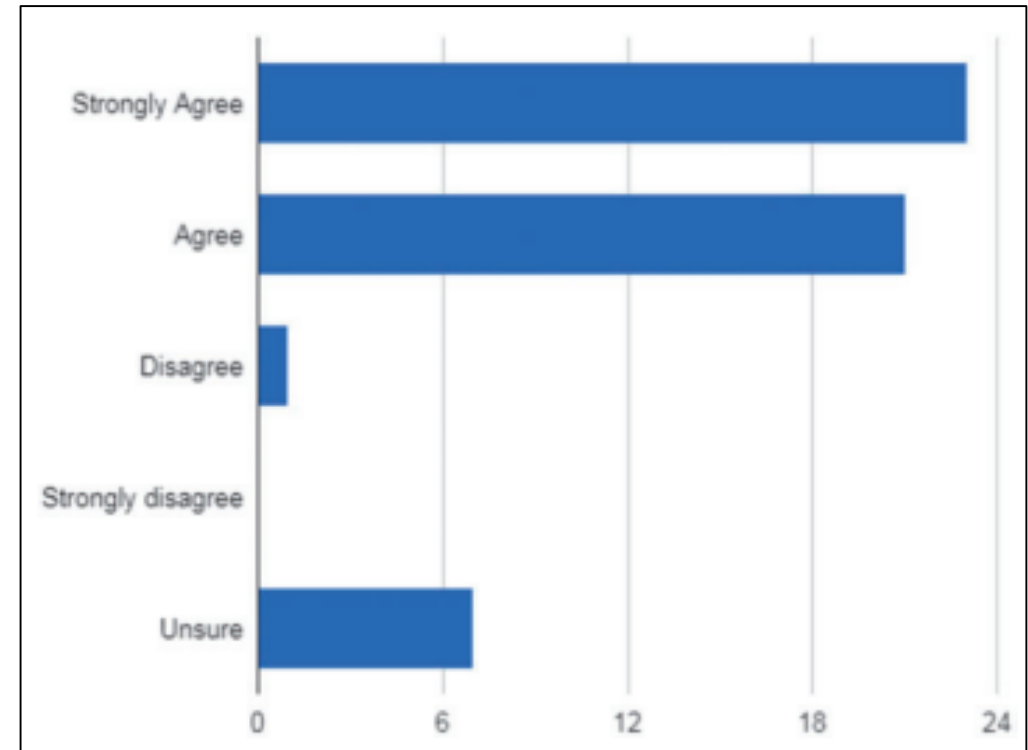
WHAT CANNOT BE DONE !

	Traditional visit	Video visit
Medical history	✓	✓
Assessment of clinical parameters:		
Weight	✓	✓
Blood pressure (BP)	✓	✓
Heart rate (HR)	✓	✓
Drug intake compliance	✓	✓
Other comorbidity parameters (e.g., glucose levels through glucometer for diabetic patients)	✓	✓
Physical examination	✓	×
Evaluation of hematochemical exams	✓	✓
Drug dosage evaluation	✓	✓
Evaluation of instrumental examinations organ's functionality assessment:		
Kidney US	✓	×
Ecocolordoppler (to be carried out at the TC)	✓	×
MRI	✓	×
Kidney biopsy (to be carried out at the TC)	✓	×
Evaluations of comorbidities:		
Instrumental examinations:		
CT scan, MRI, X-ray, US	✓	✓
DXA	✓	✓
ECG	✓	✓
Infectious surveillance	✓	✓
Oncological surveillance	✓	✓
Evaluation/review of the therapy	✓	✓
Drug prescription, hematochemical and/or instrumental exams	✓	✓
Prescription of specialist examinations	✓	✓
Training on pathology, therapy and lifestyle	✓	✓
Scheduling future appointments	✓	✓
Archiving the examination report	✓	✓

TELE-CONSULTATION AND KT : PATIENT SATISFACTION



“I felt I received same standard of care as I would have from a face-to-face appointment”



“The telehealth appointment helped me better understand my healthcare condition”

II- KIDNEY GRAFT FOLLOW-UP

1- RENAL FUNCTION MONITORING

KIDNEY ALLOGRAFT FUNCTION MONITORING



8: MONITORING KIDNEY ALLOGRAFT FUNCTION

8.1: We suggest measuring urine volume (2C):

- every 1–2 h for at least 24 h after transplantation (2D);
- daily until graft function is stable. (2D)

8.2: We suggest measuring urine protein excretion, (2C) at least:

- once in the first month to determine a baseline (2D);
- every 3 months during the first year (2D);
- annually, thereafter. (2D)

8.3: We recommend measuring serum creatinine, (1B) at least:

- daily for 7 days or until hospital discharge, whichever occurs sooner (2C);
- 2–3 times per week for weeks 2–4 (2C);
- weekly for months 2 and 3 (2C);
- every 2 weeks for months 4–6 (2C);
- monthly for months 7–12 (2C);
- every 2–3 months, thereafter. (2C)

8.3.1: We suggest estimating GFR whenever serum creatinine is measured, (2D) using:

- one of several formulas validated for adults (2C); or
- the Schwartz formula for children and adolescents. (2C)

KIDNEY ALLOGRAFT FUNCTION MONITORING



BOX 16: Post-KT monitoring of graft function

- We suggest monitoring graft function by measuring the urine volume, urinary protein excretion, serum creatinine (and eGFR), and performing US examination at a decremented frequency with progression of post-KT duration (Table 7).



Table 7. Suggested schedule for monitoring of graft function.

	First 24 h	Hospital stay	Month 1	Months 2–3	Months 4–6	Annual	Recommendation
Urine volume (2 C)	Every 1–2 h	daily	As necessary for the management of complications				1D
Urinary protein:creatinine ratio (2 C)			@month 1	@month 3	@month 6	@month 6	2D
Serum creatinine (1B) eGFR (2D)	Twice	daily	2–3/week	weekly	/2 weeks	/1–3 months	2 C
Ultrasonography (2 C)	Once		Once		Once	Once	2D

A- GFR ESTIMATE

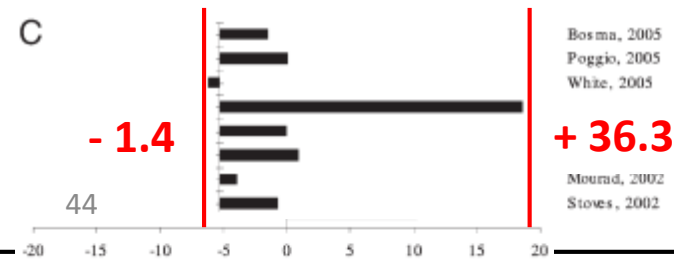
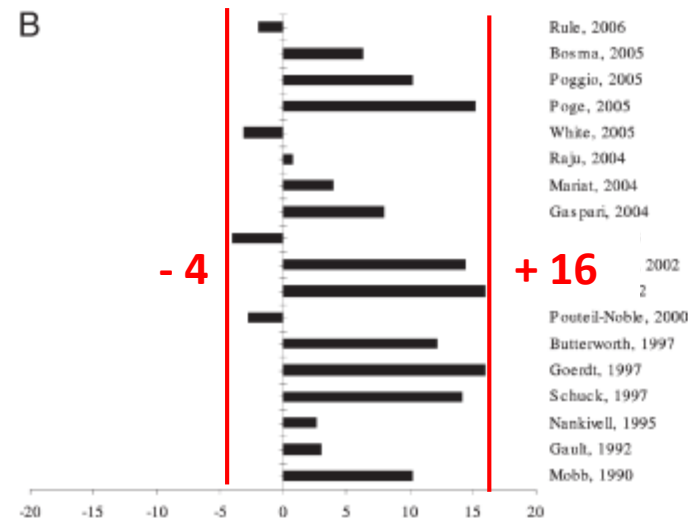
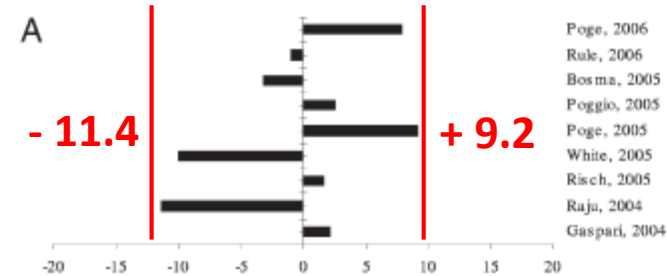
GFR ESTIMATE

Table 1 GFR equations

Years	Authors	GFR equations (ml/min/1.73 m ²)
1971	Jelliffe	$GFR = 98 - [0.8 \times (age - 20)/\text{serum creat.} \times (\text{body mass}/1.73) \times [0.9 \text{ if a woman}]$
1974	Kampmann	$GFR = \text{urine creatinine (mg/kg/min)} \times \text{weight (kg)} \times 100/\text{serum creatinine (mg/100 ml)}$
1976	Rowe	$GFR = 133 - 0.64 \times \text{age}$
1976	Cockcroft	$GFR = (140 - \text{age}) \times \text{weight} (\times 0.85 \text{ if a woman})/(\text{serum creat} \times 72)$
1987	Keller	$GFR = 130 - \text{age}$
1993	Walser	$GFR = 7.57 \times (\text{Serum Cre mmol/L})^{-1} - 0.103 \times \text{age} + 0.096 \times \text{weight}^{-6.66}$
1995	Nankivell	$GFR = 6.7/\text{Serum Cre (mmol/L)} + 0.25 \times \text{weight} - 0.5 \times \text{urea} - 0.01 \times \text{height}^2 + 35$ (25 if a woman)
1997	Baracksky	$GFR = 1/2 [100/\text{Serum Cre}] + 88 - \text{age}$
1999	MDRD	$GFR = 170 \times [\text{Serum Cre}]^{-0.999} \times [\text{age}]^{-0.175} \times [0.762 \text{ if a woman}] \times$ $[1180 \text{ if an african american}] \times [\text{BUN}]^{-0.170} \times [\text{Alb}]^{+0.318}$
2007	MDRD-6	$GFR = 170 \times (\text{creatinine}/88.4)^{-0.999} \times (\text{age})^{-0.176} \times (\text{urea} \times 2.8)^{-0.170} \times$ $(\text{albumin}/10)^{0.318} \times (0.762 \text{ if a woman}) \times (1180 \text{ if African American})$
2007	Lund-Malmö	$eX = 0.00705 \times \text{age} + 0.0110 \times \text{LBM}$ X: $4.93 - 0.0108 \times \text{serum creat (if serum creat} < 150 \mu\text{mol/L)}$ X: $7.78 - 0.0005 \times \text{serum creat} - 0.902 \times \ln(\text{serum creat})$ (if serum creat $\geq 150 \mu\text{mol/L}$)
2009	CKD-EPI	$GFR = 141 \times \min(\text{Scr}/k, 1)^\alpha \times \max(\text{Scr}/k, 1)^{-1.209} \times 0.993^{\text{edad}} \times 1.018$ [if a woman] where Scr is serum creatinine, k is 0.7 for women and 0.9 for men, $\alpha = 0.329$ for women and -0.411 for men
2010	DAF	$GFR = 80/\text{serum creat. (70 if a woman)}$
2011	Gregori-Macías	$GFR = 480.7902/\text{serum creatinine}^{0.513288} \times 1.008072^{\text{age}} \times \text{weight}^{0.298963}$
2012	BIS1	$GFR = 3736 \times \text{creatinine}^{-0.87} \times \text{age}^{-0.95} \times 0.82$ (if female)

eGFR EQUATIONS AFTER KT :

BIASES AND ACCURACY

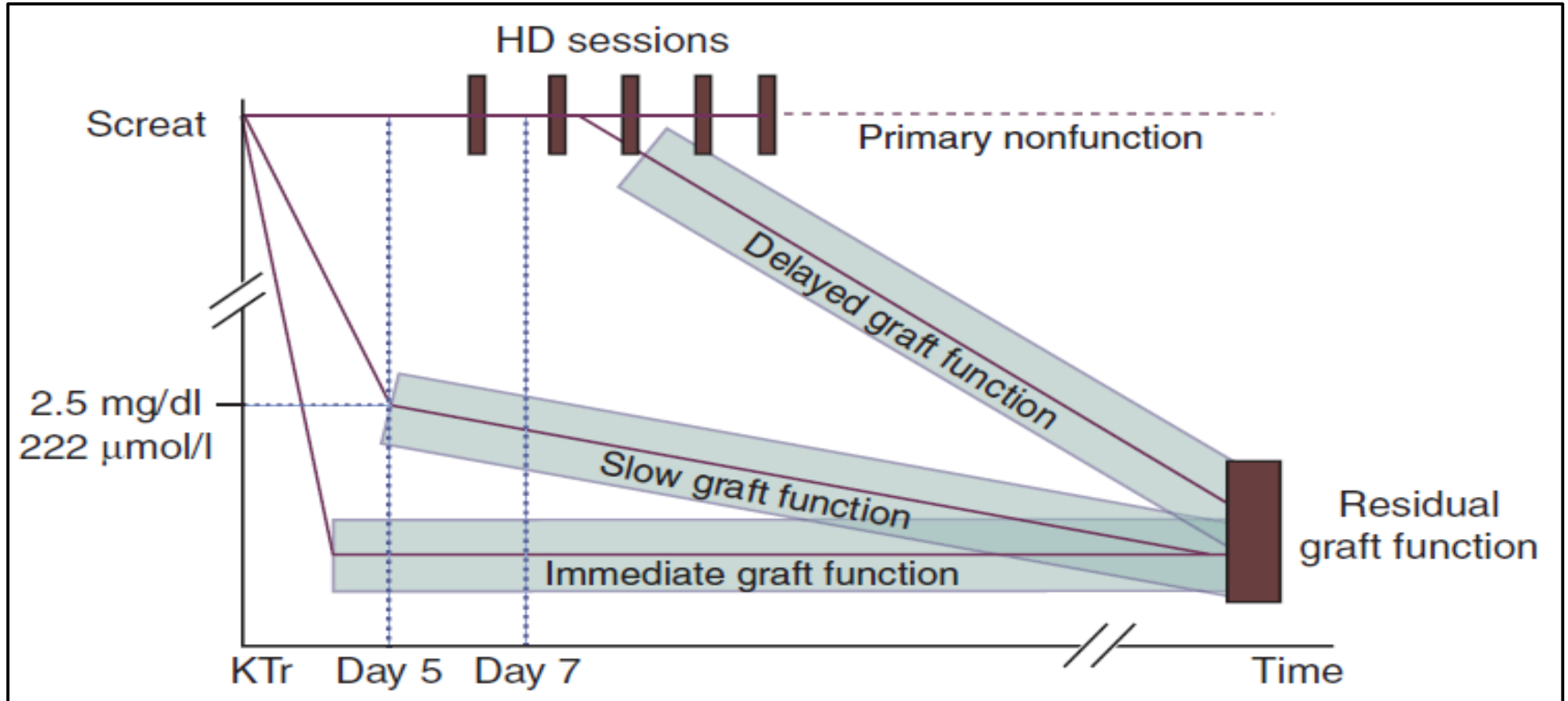


Equations and Studies	Percent of Estimates Within		
	10%	20%	30%
4-Variable MDRD Study equation			
Pooled estimate (95% CI)			
All studies	35 (32-38)	59 (54-65)	76 (74-78)
High quality*	34 (32-37)	53 (46-60)	77 (75-79)

Cockcroft-Gault equation			
Pooled estimate (95% CI)			
All studies	30 (28-32)	45 (41-48)	73 (71-75)
High quality*	32 (30-35)	37 (31-44)	73 (71-76)

Nankivell equation			
Pooled estimate (95% CI)			
All studies	31 (28-33)	42 (39-46)	68 (65-70)
High quality*	38 (32-45)	35 (32-38)	76 (74-79)

RENAL FUNCTION RECOVERY AFTER KIDNEY TRANSPLANTATION



eGFR TRAJECTORIES AND GRAFT/PATIENT SURVIVAL PREDICTION

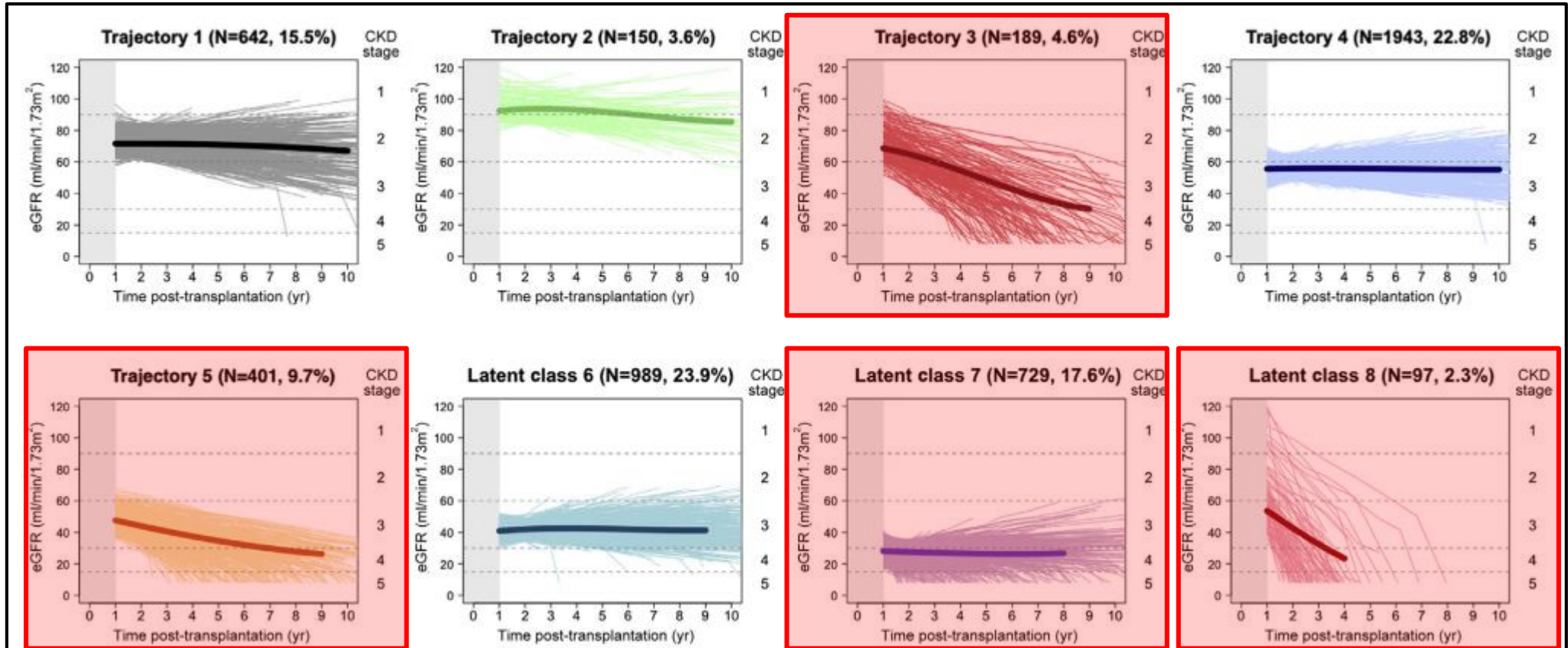


Figure 1 | (a) Estimated glomerular filtration rate (eGFR) profiles and their individual trajectories in kidney recipients in the derivation cohort.

B- GFR MEASURE

KIDNEY ALLOGRAFT GFR MEASUREMENT

■ Exogenous substances used :

✓ **Inulin** : the 1st substance used, *gold standard*

✓ Radio-pharmaceutical substances :

➤ Diethylene-triamino-penta-acetate labeled with Technetium (**^{99m}TcDTPA**)

➤ Iothalamate marked with Iodine (**¹²⁵I-iothalamate**)

➤ Ethylene-diamine-tetra-acetic acid labeled with Chromium 51 (**⁵¹CrEDTA**)

✓ Iodine contrast agents : **Iohexol**

White CA. AJKD 2008;51(6);1005-15.

Lacour B. Rev Francoph Lab. 2013;2013(451):25-37.

2- ANATOMICAL MONITORING

KIDNEY ALLOGRAFT ANATOMICAL MONITORING



8: MONITORING KIDNEY ALLOGRAFT FUNCTION

8.4: We suggest including a kidney allograft ultrasound examination as part of the assessment of kidney allograft dysfunction. (2C)

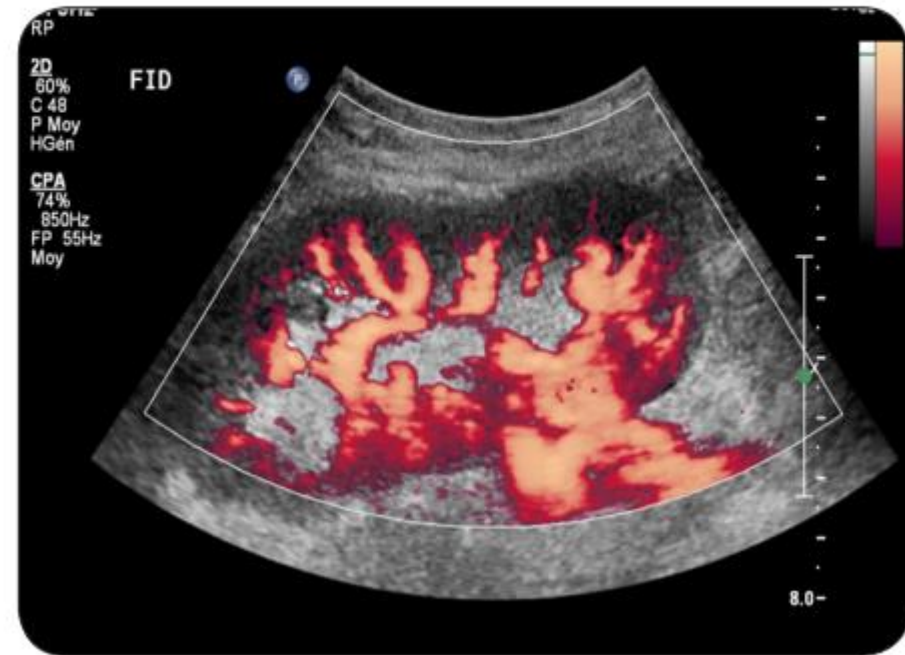
KIDNEY ALLOGRAFT ANATOMICAL MONITORING :

DOPPLER ULTRASOUND

Figure 1. Morphologie, taille et différenciation parenchymo-sinusale du greffon normal – Echographie standard.



Figure 2. Perfusion normale du parenchyme du rein greffé en doppler puissance.



KIDNEY ALLOGRAFT ANATOMICAL MONITORING : DOPPLER ULTRASOUND

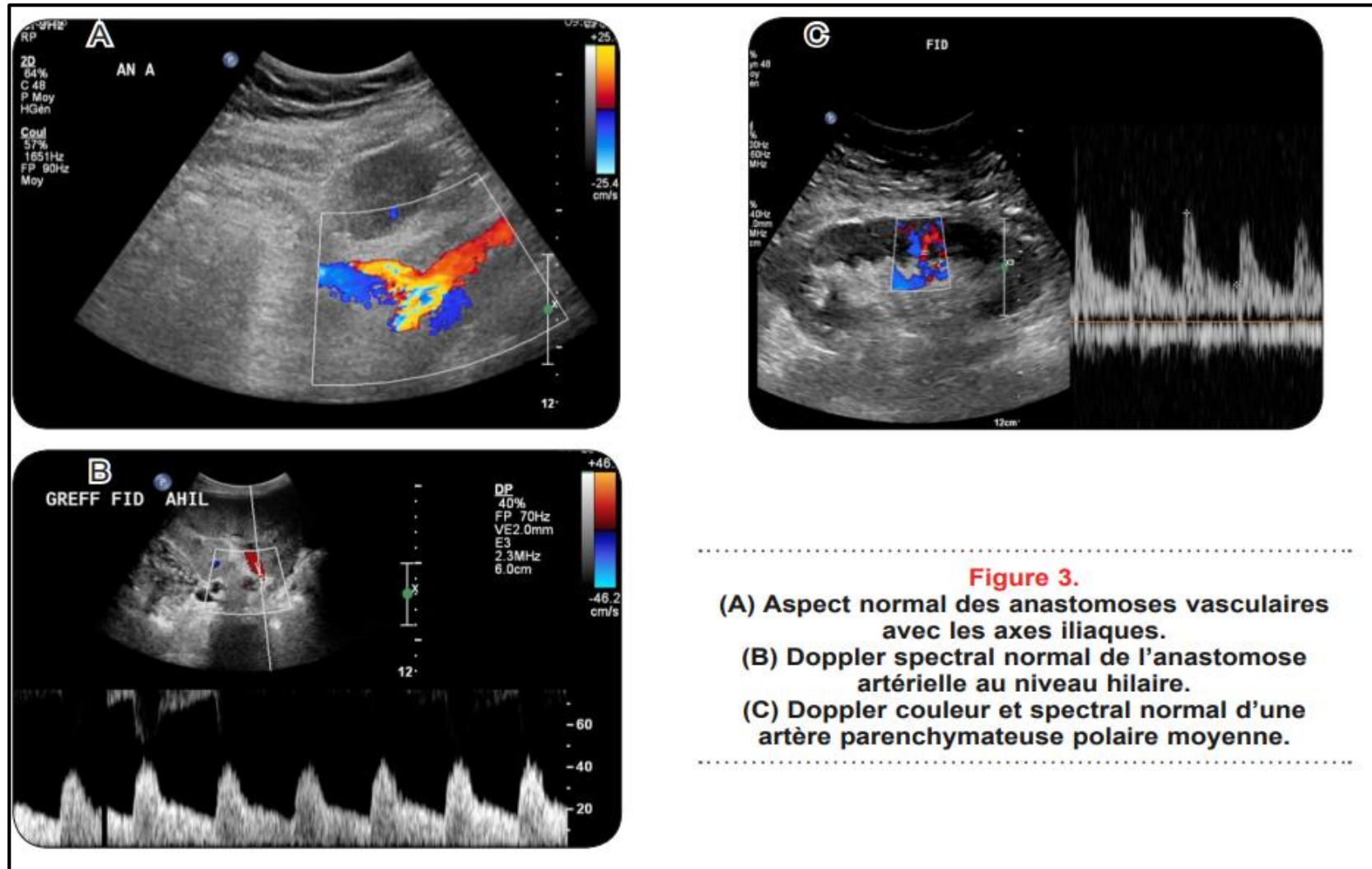


Figure 3.

- (A) Aspect normal des anastomoses vasculaires avec les axes iliaques.
- (B) Doppler spectral normal de l'anastomose artérielle au niveau hilaire.
- (C) Doppler couleur et spectral normal d'une artère parenchymateuse polaire moyenne.

KIDNEY ALLOGRAFT ANATOMICAL MONITORING : FIBROSCAN

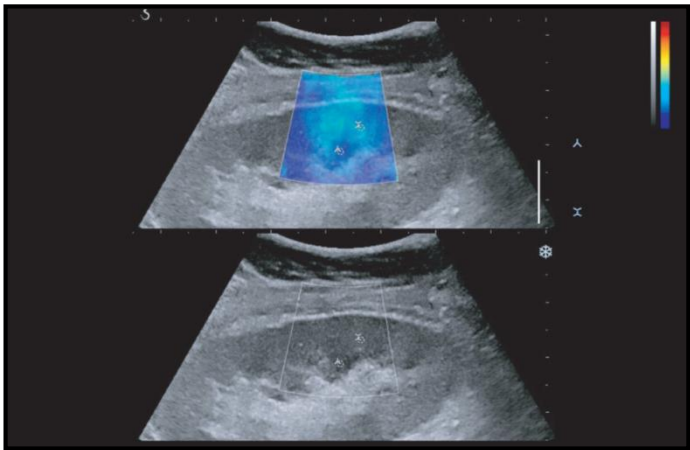


Fig. 1 SWE of a graft kidney. The upper panel is the color-coded elasticity map scaled from 0 to 60 kPa. The lower panel is the simultaneous grayscale ultrasound image. The regions of interest are placed in the cortex (X) and the medulla (A).

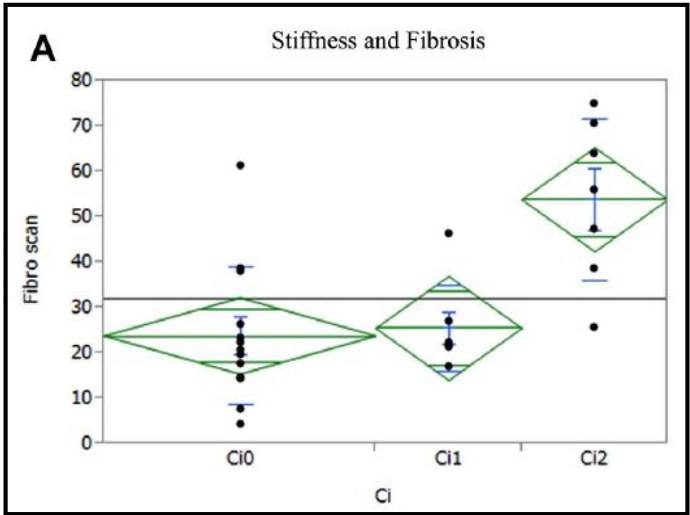
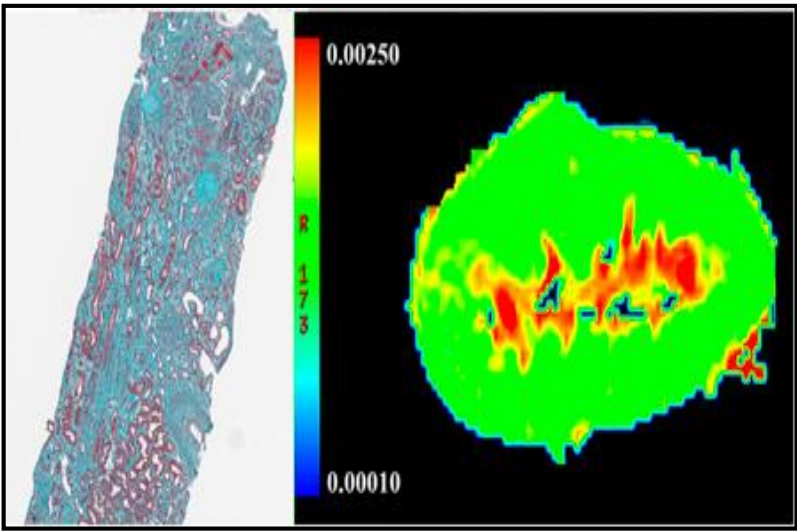
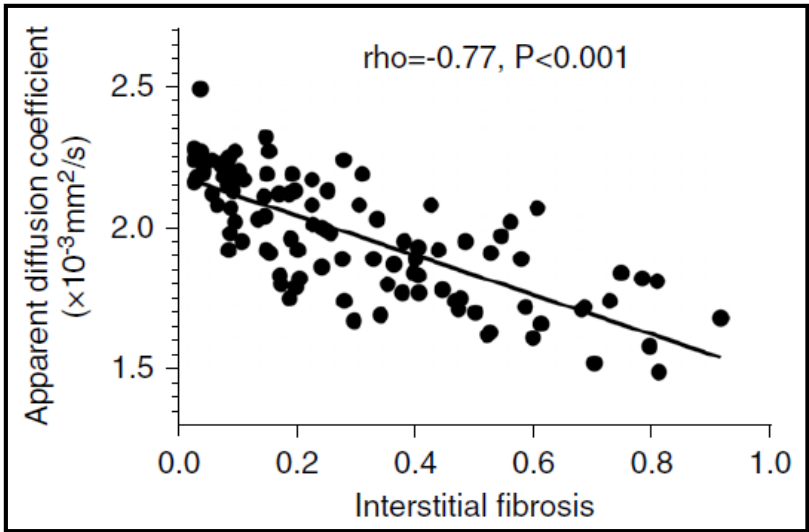
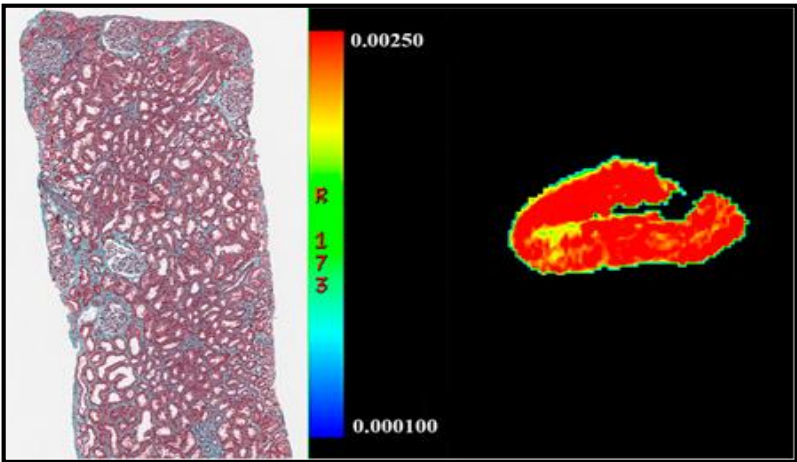
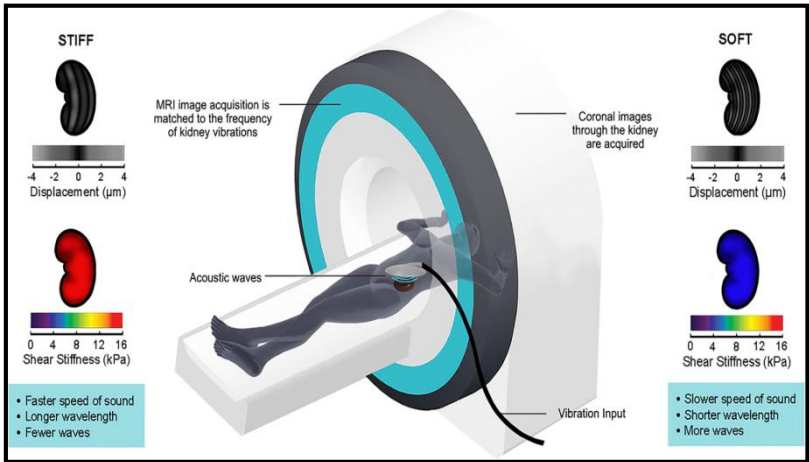


Fig. 2. (A) Comparison of stiffness values and chronic allograft injury Banff chronic changes in the interstitium grades.



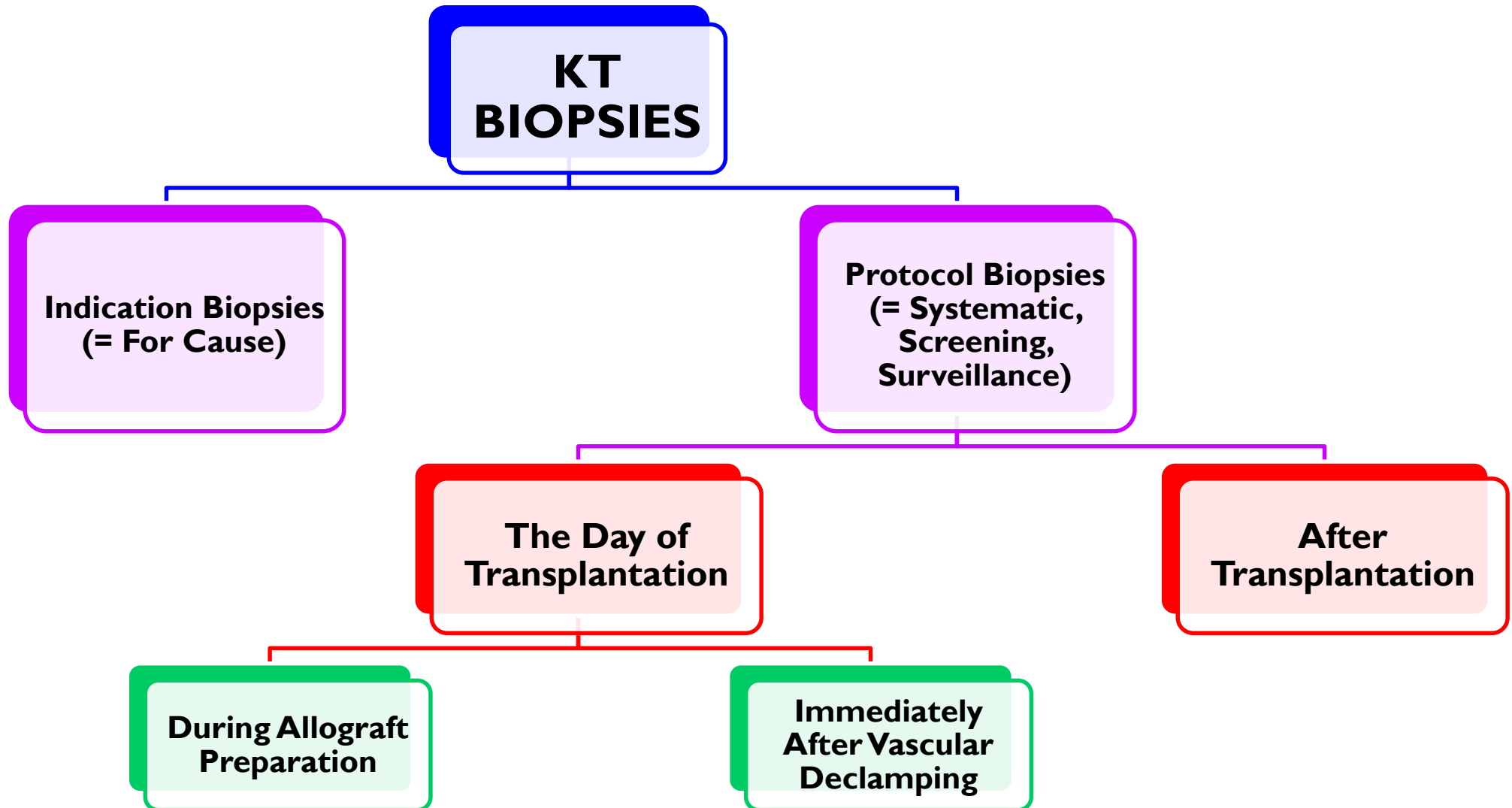
Fig 1. The transient elastography machine (Fibro Scan), which measures organ stiffness. The cylinder is 10 mm wide and 25 to 30 mm long.

KIDNEY ALLOGRAFT ANATOMICAL MONITORING : MRI ELASTOGRAPHY



3- HISTOLOGICAL MONITORING

KIDNEY TRANSPLANT BIOPSIES



INDICATION BIOPSIES

Guideline 5.7 – KTR: Renal biopsy in chronic allograft injury

We suggest that a renal transplant biopsy is indicated:

- If there is a persistent unexplained elevation of creatinine or failure to return to baseline after an episode of biopsy proven acute rejection (BPAR) (1C)
- Every 7-10 days during delayed graft function (DGF) (2C)
- If expected renal function is not achieved within 4-8 weeks (2D)
- If sustained new onset proteinuria develops (PCR >50 mg/mmol or ACR >35 mg/mmol) (2C)

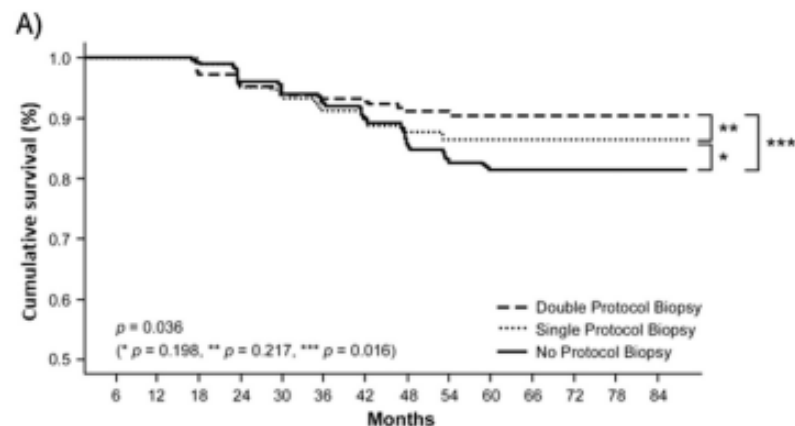
PROTOCOL BIOPSIES



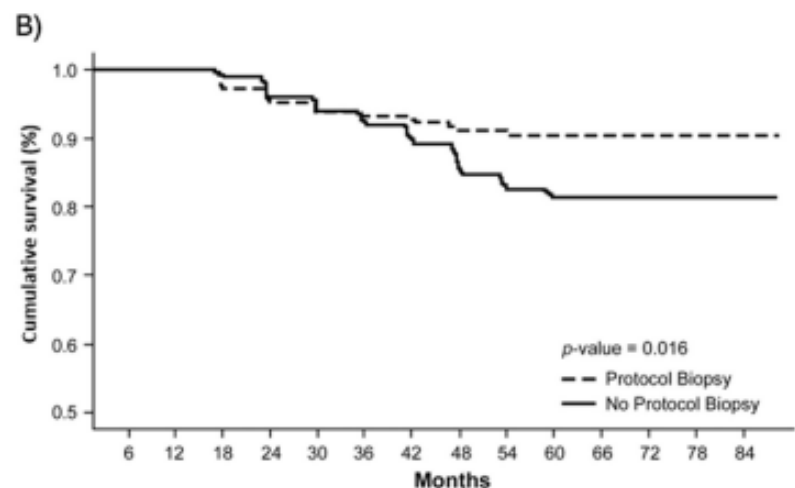
BOX 18: Protocol/surveillance biopsy

- We suggest that all very-high- and high-risk KTRs undergo a scheduled graft biopsy (with staining for C4d) at 3–6 months post-KT and 1–3 times thereafter for the first 2 years (NG).
- We suggest at least one graft biopsy (with staining for C4d) in intermediate-risk KTRs during the first year [59] (NG).
- We suggest that any KTR with detected *de novo* DSA, or with one biopsy confirmed ABMR episode or evidence of non-adherence to undergo at least one protocol biopsy (NG).
- We suggest that a protocol biopsy be obtained prior to a shift in the maintenance immunosuppression protocol and at 3 months thereafter (NG).
- We suggest that a protocol biopsy to be obtained in KTRs with a high risk of recurrence of their original disease (NG).

BENEFITS OF PROTOCOL BIOPSIES



--- 297 296 296 289 283 278 240 202 158 118 106 93 78 49 26
..... 207 206 206 204 197 193 183 174 162 146 130 100 58 40 23
— 350 349 349 347 335 328 322 312 299 289 285 285 285 285 285



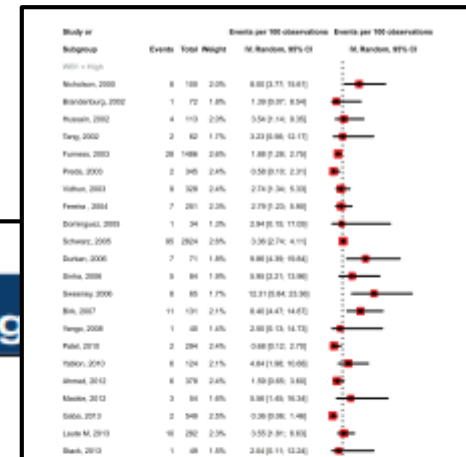
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— 350 349 349 347 335 328 322 312 299 289 285 285 285 285 285

Fig 3. Kaplan-Meier curve for CKD progression analysis between 3 groups (A) and 2 groups (B).

Table 5. Cox Regression Hazard Model for Risk Factor Analysis of Graft Survival

Characteristics	Multivariable HR (95% CI)	P Value
Recipient		
Age		
Sex (male)	1.257 (0.828-1.910)	.283
Diabetes (+)	1.803 (1.162-2.797)	.009
Hypertension (+)		
Donor		
Age	1.007 (0.990-1.025)	.411
Sex (male)		
Diabetes (+)	1.076 (0.536-2.161)	.837
Hypertension (+)	1.149 (0.651-2.025)	.632
Creatinine		
High HLA I mismatch (≥ 3)		
High HLA II mismatch (≥ 2)		
Donor specific antigen		
ABO-incompatible KT		
Induction (rATG)	1.320 (0.844-2.067)	.224
DDKT	1.181 (0.738-1.891)	.489
Rejection episode	2.757 (1.815-4.188)	<.001
Post-KT GN	4.048 (2.685-6.101)	<.001
Protocol biopsy		
Single biopsy	1.106 (0.628-1.947)	.728
Double biopsy	0.451 (0.229-0.888)	.021
CMV ($\geq 50/400,000$)	1.278 (0.734-2.225)	.385
BKV nephritis		

COMPLICATIONS OF KT BIOPSIES



**Macroscopic Hematuria
3.18 %**

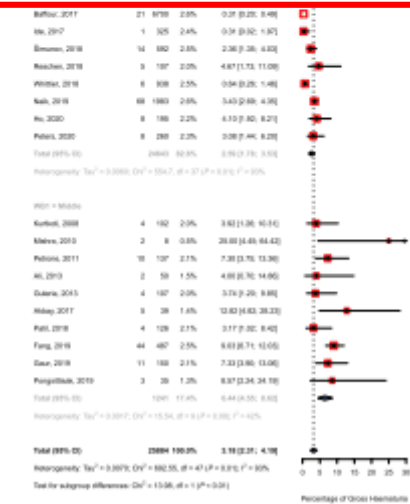
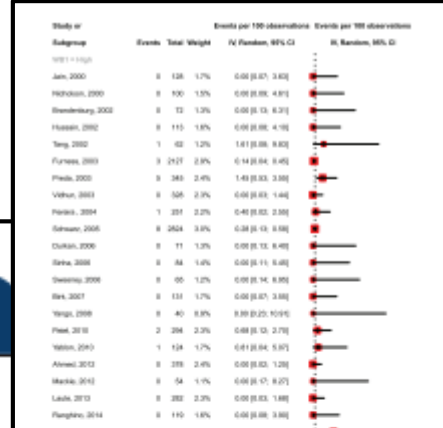


FIGURE 2. Forest plot showing incidence of gross hematuria after percutaneous kidney allograft biopsy. CI, confidence interval; df, degree of freedom.



**Bleeding Requiring
Transfusion
0.31 %**

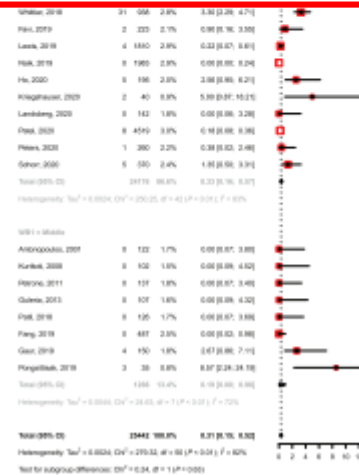
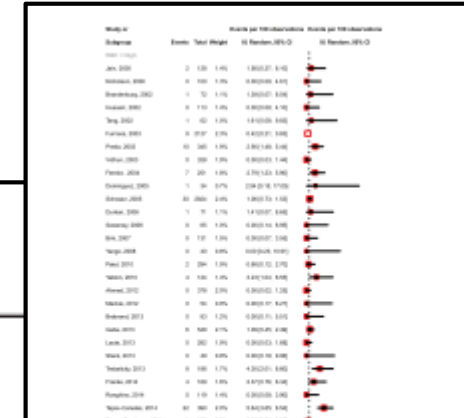


FIGURE 3. Forest plot showing incidence of need for blood transfusion after percutaneous kidney allograft biopsy. CI, confidence interval; df, degree of freedom.



**Major Complications
0.89 %**

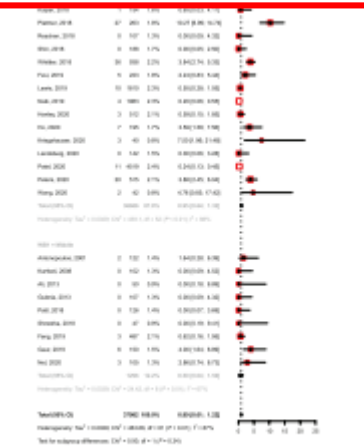


FIGURE 4. Forest plot showing incidence of major complications after percutaneous kidney allograft biopsy. CI, confidence interval; df, degree of freedom.

4- BIOMARKERS

CLINICAL UTILITY OF BIOMARKERS

TABLE 3 Selected biomarkers and their clinical utility in kidney transplantation

Biomarkers	Potential clinical use
IFN- γ	Predicts rejection risk For risk stratification and selection of immunosuppression
IL-2	Predicts rejection risk For risk stratification and selection of immunosuppression
Serum soluble CD30	Predicts long-term allograft outcome
T cells CD26 and CD28 surface antigens	Associated with acute rejection and/or malignancy after transplantation
Regulatory T cells	Predicts acute rejection risk
Target enzyme activity: IMPDH	May predict acute rejection risk or MPA-associated side effects Better guide MPA therapy
Target enzyme activity: mTOR	Better guide mTOR inhibitor therapy
NFAT-regulated gene expression	May identify those at higher risk of acute rejection, opportunistic infections, cancers and cardiovascular risk Complements CNI pharmacokinetics to better guide CNI therapy
CXCs	Urinary CXCL-9 and CXCL-10 proteins as markers for kidney graft inflammation and alloimmune response Urinary CCL-2 as marker for inflammation and interstitial fibrosis in renal allografts
dd-cfDNA	Early detection of graft injury due to rejection, specific infections, or ischemia Serial dd-cfDNA determinations help to guide changes in immunosuppression, and to monitor minimization
CYP3A5	May help to determine the optimal starting tacrolimus dose

Abbreviations: CNI, calcineurin inhibitor; CXC, chemoattractant cytokines or chemokines; CYP, cytochrome P450; Donor-derived cell-free DNA, dd-cfDNA; IFN, interferon; IL, interleukin; IMPDH, inosine-monophosphate-dehydrogenase; MPA, mycophenolic acid; NFAT, Nuclear Factor of Activated T-Cell; mTOR, mammalian target of rapamycin.

BIOMARKERS OF ACUTE REJECTION :

IL-23 AND IL-17

DOI: 10.1002/JLB.5AB0318-148R

J Leukoc Biol. 2018;104:1229–1239.

JLB JOURNAL OF
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BIOLOGY

BRIEF CONCLUSIVE REPORT

The role of IL-23/IL-17 axis in human kidney allograft rejection

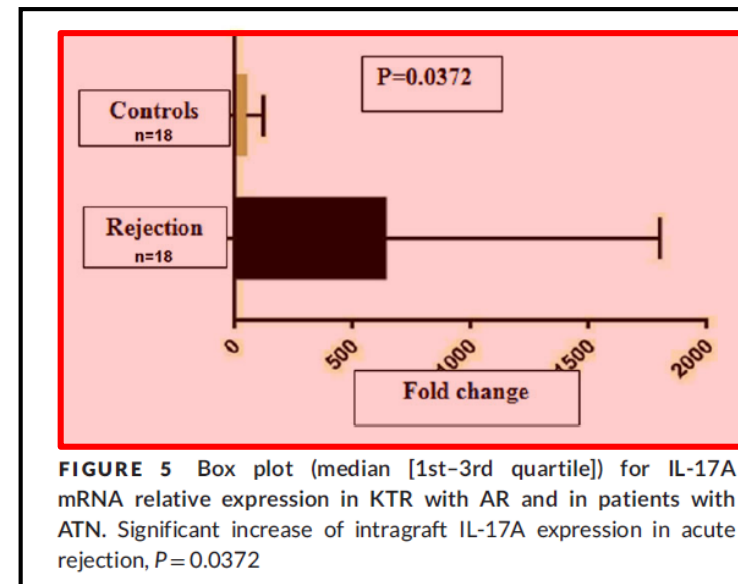
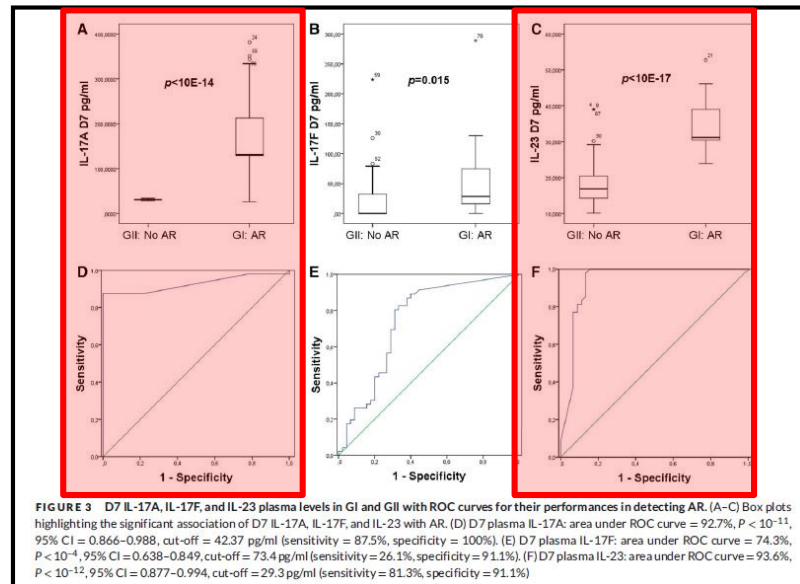
Youssra Haouami¹ | Tarak Dhaouadi¹ | Imen Sfar¹ | Mongi Bacha^{1,2} |
Tahar Gargah^{1,3} | Rafika Bardi¹ | Ezzeddine Abderrahim^{1,2} | Rym Goucha^{1,2} |
Taïeb Ben Abdallah^{1,2} | Yousr Gorgi¹

BIOMARKERS OF ACUTE REJECTION :

IL-23 AND IL-17

TABLE 3 Cytokine plasma levels in patients (GI) and controls (GII)

Cytokine	D-1			D7		
	GI	GII	P-value	GI	GII	P-value
IL-17A (pg/ml)	79.407	31	0.00022 ^a	157.455	31.1	<10 ⁻¹⁴ ^b
IL-17F (pg/ml)	38.041	28.87	0.323	47.86	22.99	0.015 ^c
IL-23 (pg/ml)	35.752	37.204	0.197	33.82	18.811	<10 ⁻¹⁷ ^d
Cytokines' evolution in GI						
	D-1			D7		P-value
IL-17A (pg/ml)	79.407			157.455		<10 ^{-4e}
IL-17F (pg/ml)	38.041			47.86		0.323
IL-23 (pg/ml)	35.752			33.82		0.163



BIOMARKERS OF EMT/ALLOGRAFT FIBROSIS : VIMENTIN, CD45, UROPLAKIN



m/s
médecine/sciences

médecine/sciences 2015 ; 31 : 68-74
DOI : 10.1051/medsci/20153101015

La transition épithélio-mésenchymateuse et la fibrose du transplant rénal

Imen Mezni^{1,2}, Pierre Galichon^{1,3},
Mohamed Mongi Bacha^{2,5}, Imen Sfar²,
Alexandre Hertig^{1,3}, Rim Goucha^{2,5},
Yi-Chun Xu-Dubois¹, Ezzedine Abderrahim⁵,
Yours Gorgi², Eric Rondeau^{1,3}, Taieb Ben Abdallah^{2,5}

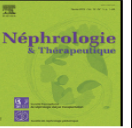
> La transition épithélio-mésenchymateuse (TEM) est un processus par lequel les cellules épithéliales différenciées subissent une conversion phénotypique et acquièrent un phénotype de cellules mésenchymateuses. Outre la morphologie allongée, s'y associent une

Néphrologie & Thérapeutique 14 (2018) 153–161



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Original article

Urinary mRNA analysis of biomarkers to epithelial mesenchymal transition of renal allograft

Imen Mezni^{a,b,d,*}, Pierre Galichon^{a,b,c}, Mohammed Mongi Bacha^{d,g}, Yi-Chun Xu-Dubois^{b,e}, Imen Sfar^d, David Buob^{a,b,f}, Sabrina Benbouzid^h, Rim Goucha^{d,g}, Yours Gorgi^d, Ezzedine Abderrahim^g, Mondher Ounissi^g, Karine Dahanⁱ, Nacera Ouali^c, Alexandre Hertig^{a,b,c}, Isabelle Brocheriou^{a,b,f}, Aly Raies^j, Taieb Ben Abdallah^{d,g}, Éric Rondeau^{a,b,c}

^a Sorbonne universités, université Pierre-et-Marie-Curie, 4, place Jussieu, 75005 Paris, France
^b Inserm UMR_S1155, hôpital Tenon, 4, rue de la Chine, 75020 Paris, France
^c Urgences néphrologiques et transplantation rénale, hôpital Tenon, 4, rue de la Chine, 75020 Paris, France
^d Laboratoire de recherche d'immunologie de la transplantation rénale et d'immunopathologie (LR03SP01), EPS Charles-Nicolas, boulevard du 9-Avril-1938, 1006 Tunis, Tunisia
^e Service de santé publique, hôpital Tenon, 4, rue de la Chine, 75020 Paris, France
^f Service d'anatomie pathologique, hôpital Tenon, 4, rue de la Chine, 75020 Paris, France
^g Service de médecine interne A, EPS Charles-Nicolas, boulevard du 9-Avril-1938, 1006 Tunis, Tunisia
^h Service d'urologie, hôpital Tenon, 4, rue de la Chine, 75020 Paris, France
ⁱ Service de néphrologie et dialyses, hôpital Tenon, 4, rue de la Chine, 75020 Paris, France
^j Laboratoire des microorganismes et biomolécules actives, faculté des sciences de Tunis, université de Tunis El-Manar, 20, rue de Tolède, 2092 Tunis, Tunisia

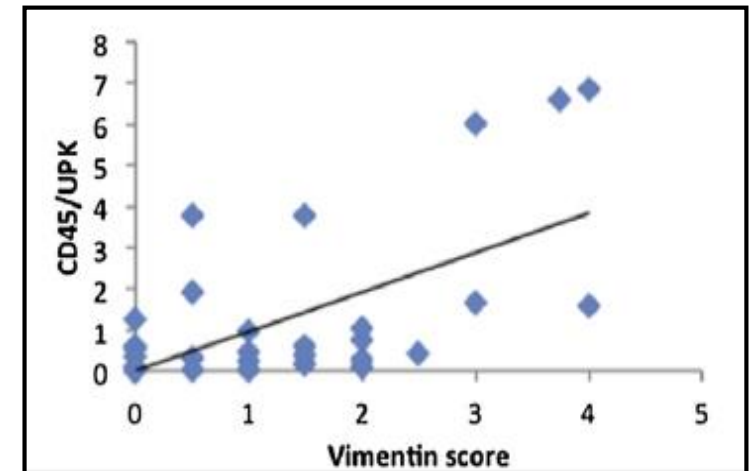
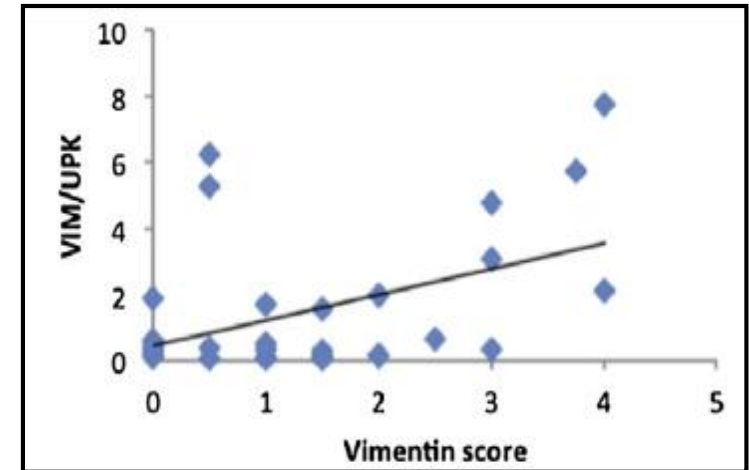


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BIOMARKERS OF EMT/ALLOGRAFT FIBROSIS :

VIMENTIN, CD45, UROPLAKIN

- Prospective, multicenter study
- Charles Nicolle Hospital, Tunis + Tenon Hospital, Paris
- 2008 - 2013
- 75 KT patients (23 living and 52 deceased donors)
- At 3 months post-KT:
 1. Vimentin and β -Catenin expression in the surveillance biopsy (immunohistochemistry)
 2. Urinary measured mRNA encoding Vimentin, CD45, GAPDH and UPK1a (quantitative PCR)



III- IMMUNOLOGICAL MONITORING

IMMUNOLOGICAL RISK STRATIFICATION

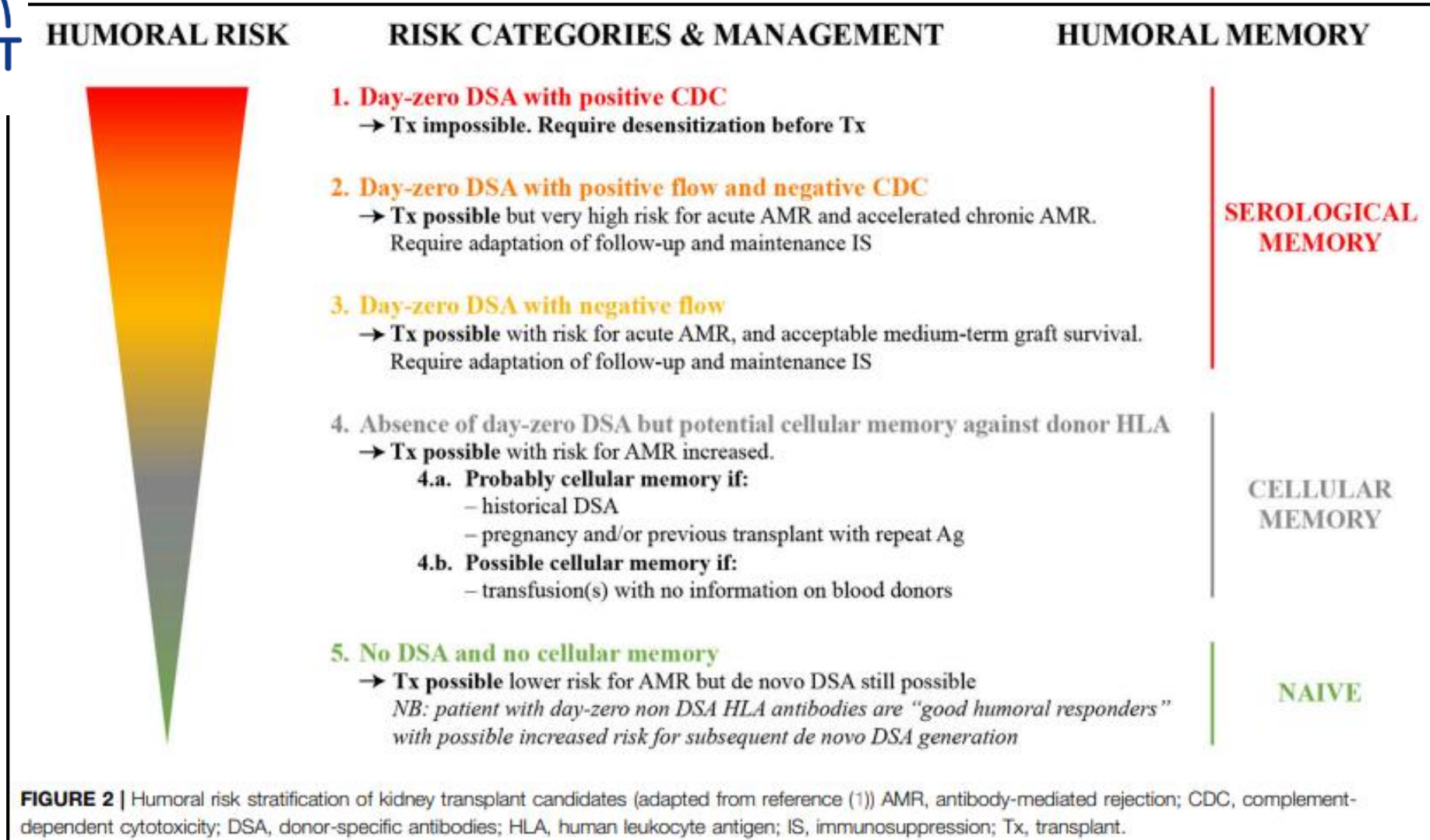


Table 3. Proposed categorisation of recipient's immunological risk.

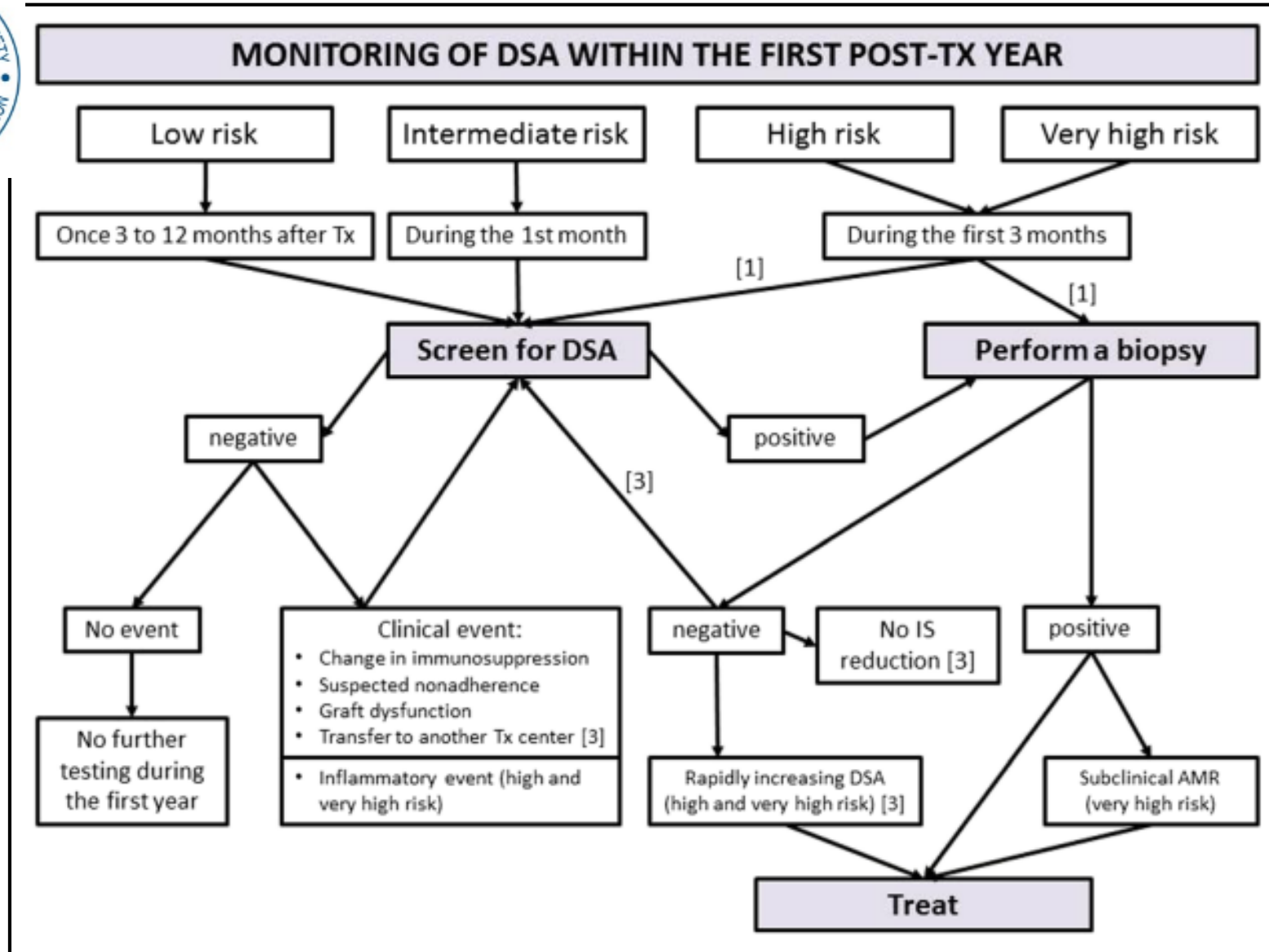
CAT	Highest risk – <i>KT is contraindicated:</i>
A	Positive CDC-XM; Positive FCM-XM MCS >250; Positive DSA RIS ≥ 17
CAT	Very High risk – <i>requires desensitisation</i>
B	Positive FCM-XM MCS ≤ 250 ; Positive DSA RIS <17; Historic positive DSA
CAT	High risk – <i>Possible desensitisation; induction mandatory; modified immunosuppression and follow-up protocol</i>
C	Previous graft failure due to rejection during first post-KT year, re-transplant, full HLA mismatches; CPRA >80% positive non-DSA anti-HLA Abs
CAT	Intermediate risk – <i>Induction, modified immunosuppression and follow-up</i>
D	Re-transplant; >3/6 HLA mismatches, CPRA 20–80%, <i>positive non DSA anti-HLA Abs</i>
CAT	Low risk – Lacking all of the above factors, proportionate to HLA matching and without anti HLA Abs
E	

CDC: complement-dependent cytotoxicity; DSA: donor-specific Abs; FCM: flow-cytometric; MCS: mean channel shift; CPRA: Calculated Panel Reactive Antibodies; RIS: Relative Mean Fluorescence Intensity (MIF) Score (10 points for each MFI $\geq 10\ 000$ + 5 points for each MFI 5000–9999 + 2 points for each MFI 2000–4999); XM: Cross-match.

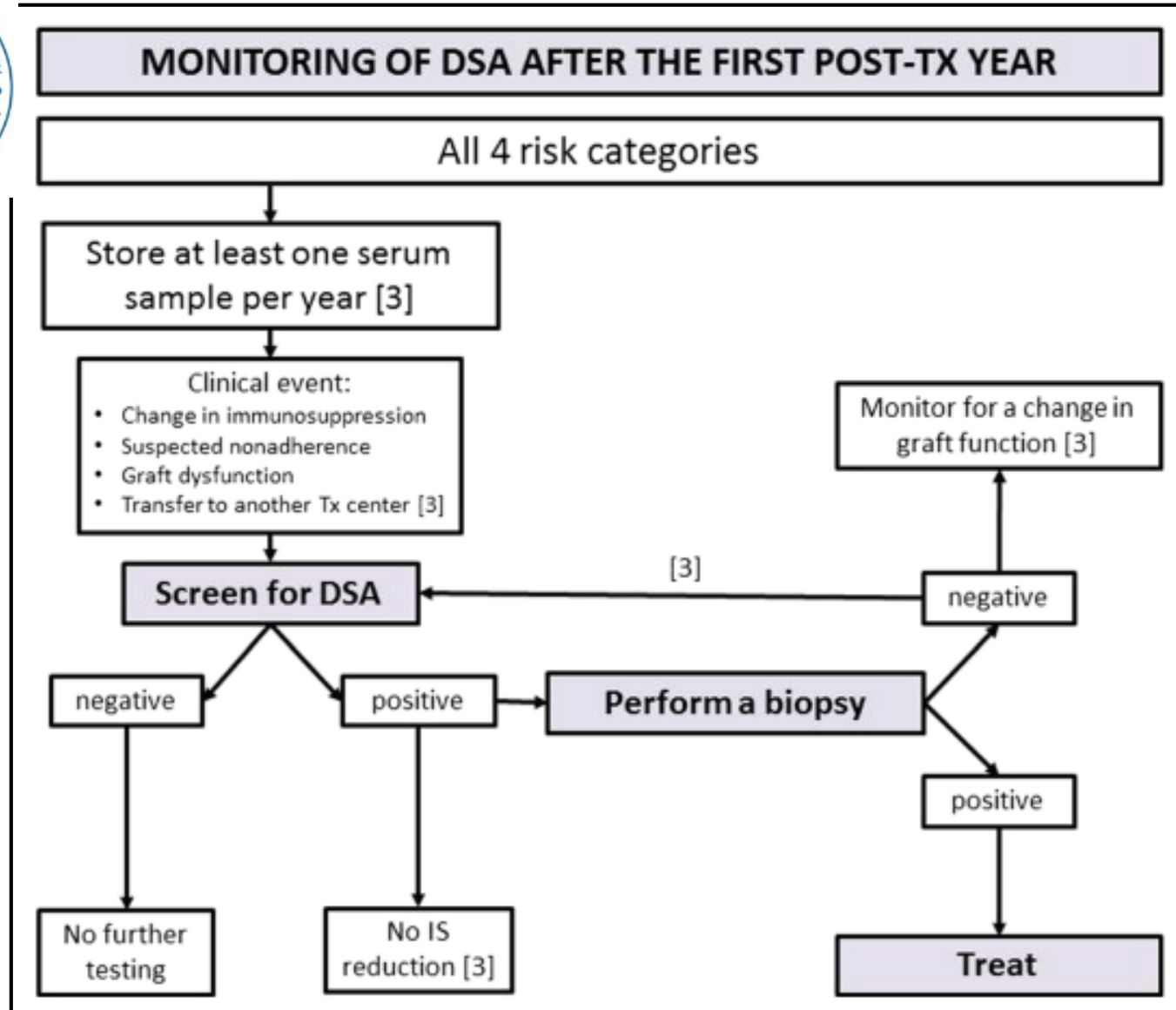
IMMUNOLOGICAL RISK STRATIFICATION



DSA MONITORING : DURING THE 1st YEAR



DSA MONITORING : AFTER THE 1st YEAR



IV- MONITORING OF IMMUNOSUPPRESSION AND ITS COMPLICATIONS

1- PHARMACOLOGICAL MONITORING

IMMUNOSUPPRESSION :

NARROW THERAPEUTIC WINDOW REQUIRING STRICT MONITORING

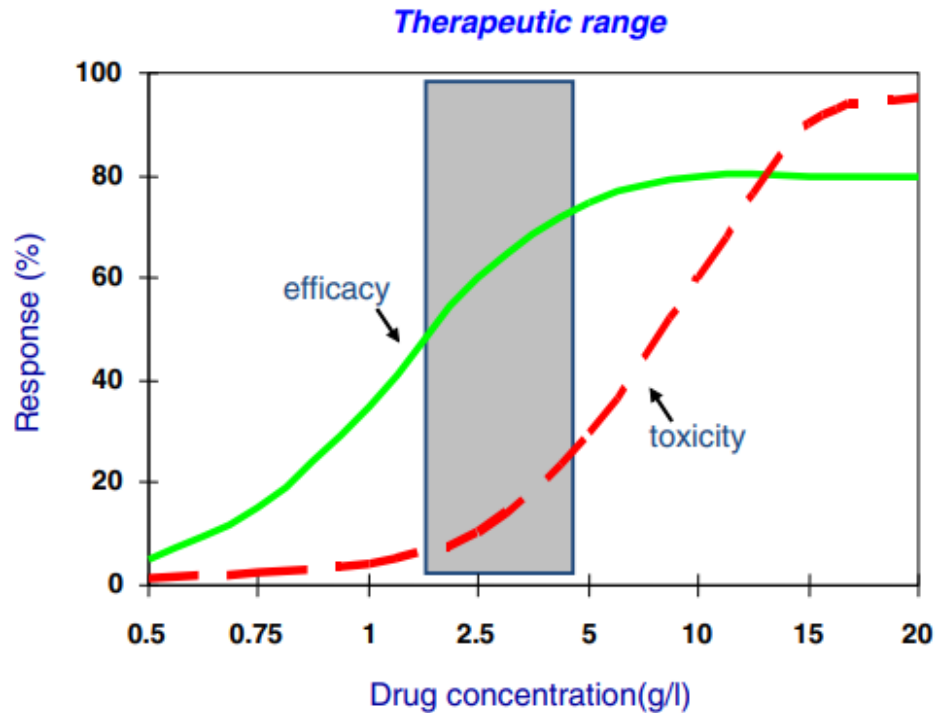


Fig. 1 Balance between efficacy and toxicity showing the narrow therapeutic range. [Courtesy (and in honor of) V.W. Armstrong (†), Göttingen, Germany]

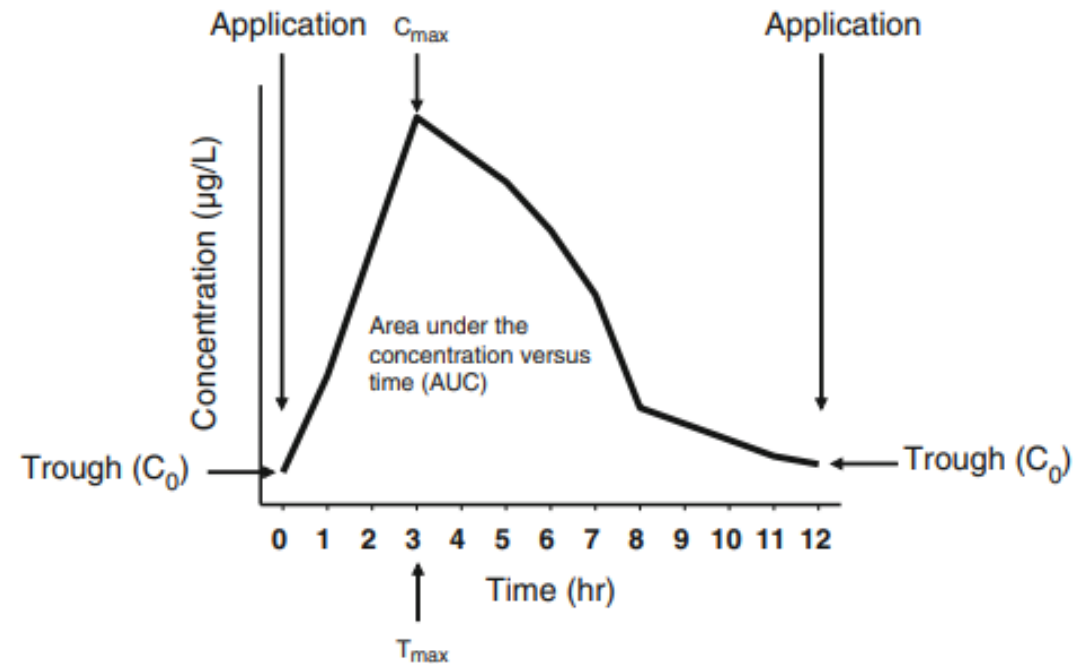


Fig. 2 Pharmacokinetic parameters during a dosing interval. C_{max} Maximum concentration, T_{max} time to maximum drug concentration, C_0 predose concentration

PHARMACOKINETIC MONITORING

Guideline 3.13 – KTR: Monitoring of immunosuppression

We suggest that long-term monitoring of immunosuppression levels is required as follows:

- Tacrolimus and ciclosporin levels should be monitored. The initial frequency should be three times a week. Levels should also be checked when any medication with possible interactions is prescribed, the dosage is changed, the formulation is changed, or when there is unexplained graft dysfunction (2C)
- Tacrolimus should be monitored by the trough (C_0) level, while ciclosporin can be monitored by either C_0 or 2-hour post dose (C_2) level (2C)
- Tacrolimus and ciclosporin levels should be available within 24 hours of taking blood samples in the first three months after transplantation (2D)
- The utility of monitoring mycophenolic acid (MPA) C_0 levels is uncertain (2D)
- Sirolimus should be monitored by the C_0 trough level (2C)

Guideline 3.17 – KTR: Prescribing and the use of generic agents

We suggest that KTRs should be closely monitored after switching between generic preparations until a new steady state is established (2D)

PHARMACOKINETIC MONITORING : CALCINEURIN INHIBITORS



Table 4. Recommended therapeutic blood levels of the calcineurin inhibitors (CNIs).

CNI		First 3 months	4–6 months	6–12 months	After 1-year rejection free	Recommendation
Tacrolimus, ng/mL	C0	8–12	5–8	5–8	5–6	2D
Cyclosporine A, ng/mL	C0	300–350	150–250	100–150	75–125	2D
	C2	1300	800–900	500–700	450–500	

C0: trough level; C2: blood level 2 h after the dose

PHARMACOKINETIC MONITORING : ANTI-METABOLITES, mTOR INHIBITORS

Table 3 (continued)

Agent	Parameter	Target range after RTx	Proposed timing of TDM In general: • After dose alteration • In case of potential drug–drug interaction • In case of suspected toxicity • In case of rejection	Specific characteristics/limited sampling strategies	Reference
Mycophenolatemofetil (MMF)	MPA predose level (C_0)	1.0–3.5 mg/L (HPLC) 1.3–4.5 mg/L (EMIT)	• Three times per week within the first 3 weeks after RTx • Once per week in weeks 4–8 after RTx • Once per month >8 weeks after RTx • At any outpatient visit in the long-term run	Reduce daily dose by 50 % in case of leukocytopenia <4,000/ μ L or neutropenia of <1,600/ μ L. Interrupt therapy in case of leukocytopenia <2,000/ μ L or neutropenia <1,300/ μ L. In case of distinct diarrhea for >3 days without different cause give daily dose t.i.d. to q.i.d. and/or reduce daily dose by 50 %	[42, 70, 71]
	MPA AUC _{0–12}	30–45–60 mg h/L (HPLC/MS) 35–52–70 mg h/L (EMIT)	• Day 3–7, days 10–14 and 3–9 months after RTx • In case of clinical change (e.g. loss of renal function, hypalbuminemia) • If necessary: TDM of free MPA in case of suspected toxicity	Calculated MPA AUC = $18.6 + 4.3 \times C_0 + 0.54 \times C_{0.5} + 2.15 \times C_2$ (+ CsA) Calculated MPA AUC = $10.0 + 3.95 \times C_0 + 3.24 \times C_{0.5} + 1.01 \times C_2$ (+ Tac or without CNI)	[39, 72, 73, 74]
Everolimus (EVR)	EVR trough level (C_0)	3–8 μ g/L 2–5 μ g/L in follow-up	Adapted to trough level monitoring of the added CNI	Dose modifications in 20 % steps after second deviation upward or downward	[4]
Sirolimus (SIR)	SIR trough level (C_0)	4–12 ng/mL (with CNI) 5–10 ng/mL (CNI-free regimen)	• Once per week during the first month • Every other month thereafter	Pay attention to dyslipidemia! Use not recommended in proteinuria.	[47]

RTx, Renal transplantation; TDM, therapeutic drug monitoring; C_{max} , maximum drug concentration, T_{max} , time to maximum concentration; C_0 , predose concentration; $C_{1–12}$, concentration a 1–12 h after administration; AUC area under the concentration–time curve; CNI, calcineurin inhibitor; HPLC, high-performance liquid chromatography; MS, mass spectrometry

^a EMIT assay, co-medication: Mycophenolatemofetil

PHARMACOKINETIC MONITORING : CALCINEURIN INHIBITORS

LA TUNISIE MEDICALE-2023; Vol 101 (10): 738-744



ARTICLE ORIGINAL

The effects of the CYP3A5*3 variant on tacrolimus pharmacokinetics and outcomes in Tunisian kidney transplant recipients

Les effets du variant CYP3A5*3 sur la pharmacocinétique du tacrolimus et le pronostic de transplantés rénaux tunisiens

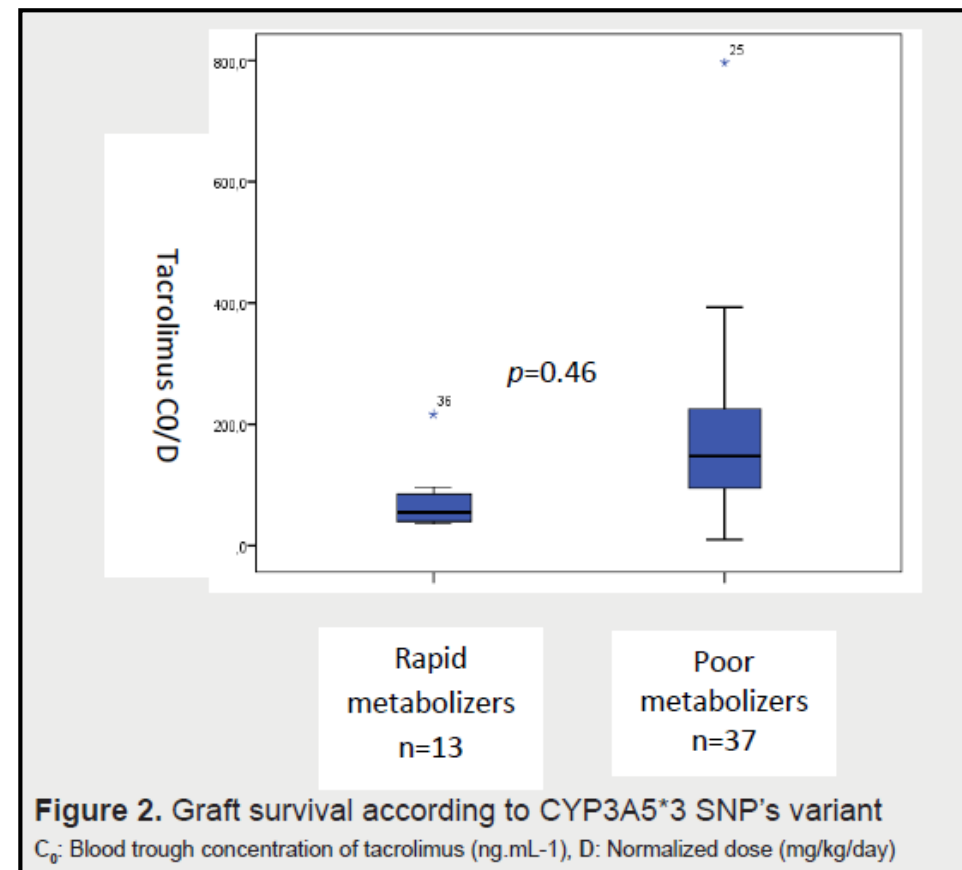
Rim Charfi¹, Mohamed Mongi Bacha², Myriam Ben Fadhla³, Khoulood Ferchichi¹, Hanene El Jebari¹, Emna Gaies¹, Anis Klouz¹, Ezzeddine Abderrahim², Fathi Ben Hamida², Taieb Ben Abdallah², Sameh Trabelsi¹, Yosr Gorgi³, Imen Sfar³

PHARMACOKINETIC MONITORING : CALCINEURIN INHIBITORS

Table 3. Pharmacokinetic parameters according to CYP3A5*3 variants (n=50).

	CYP3A5 *1/*1 and *1/*3	CYP3A5 *3/*3	p
Global results			
Genotypic frequencies	13 (26%) ^c	37 (74%) ^c	
D (mg/kg/day)	0.078 ± 0.029 ^a	0.08 ± 0.03 ^a	0.8
C ₀ [*] (ng.mL ⁻¹)	4 (3-6) ^b	7.5 (5.6-10.4) ^b	0.000
AUC _{0-12h} ^{**} (h.µg.L ⁻¹)	94 (57-148) ^b	151 (122-193) ^b	0.003
C ₀ /D	66 (40-90) ^b	98 (67-197) ^b	0.013
AUC _{0-12h} /D	1136 (960-1689) ^b	2007 (1418-3558) ^b	0.021
Results according post-transplant phases			
Early phase			
D (mg/kg/day)	0.090 ± 0.029 ^a	0.10 ± 0.03 ^a	0.3
C ₀ (ng.mL ⁻¹)	4.5 ± 3.8 ^a	7.2 ± 2.7 ^a	0.12
AUC _{0-12h} (h.µg.L ⁻¹)	112.5 ± 75.4 ^a	144.4 ± 57.5 ^a	0.3
C ₀ /D	57.7 ± 50.9 ^a	72.0 ± 45.8 ^a	0.4
AUC _{0-12h} /D	1354 ± 983 ^a	1581 ± 923 ^a	0.6
Late phase			
D (mg/kg/day)	0.075 ± 0.030 ^a	0.070 ± 0.050 ^a	0.2
C ₀ (ng.mL ⁻¹)	4.40 ± 1.97 ^a	8.46 ± 4.14 ^a	0.01
AUC _{0-12h} (h.µg.L ⁻¹)	95 ± 42 ^a	165 ± 82 ^a	0.002

AUC_{0-12h}: Area under the curve of tacrolimus, C₀: Blood trough concentration of tacrolimus, D: Daily normalized dose of tacrolimus (mg/kg/day). Data were ^a Means ± standard deviation; ^b Median [interquartile range], and ^c Number (percentage)



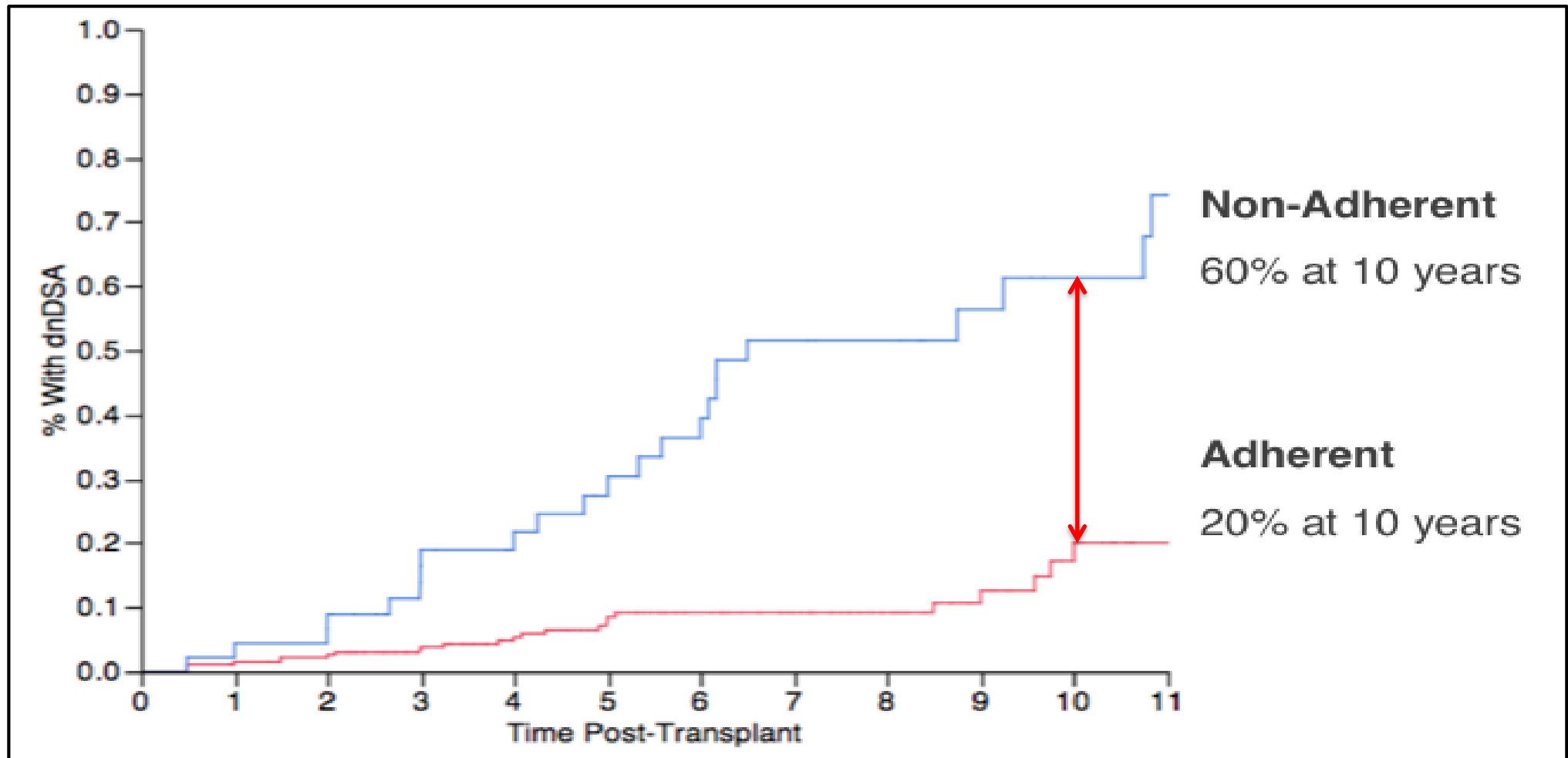
2-THERAPEUTIC ADHERENCE MONITORING

POOR THERAPEUTIC ADHERENCE : PREVALENCE

Table 2 Estimated prevalence of nonadherence in kidney transplant recipients

Study	Nonadherence measurement	Prevalence of nonadherence
Dew et al. [20]	Several methods	36 cases per 100 person-years
Germani et al. [21]	Questionnaire	18 %
Massey et al. [22]	Self-report	27 %
Schmid-Mohler et al. [23]	Self-report and collateral report	26.4 %
Denhaerynck et al. [24]	Electronic monitoring	13.2 % in Europe 19.3 % in US
Griva et al. [25]		13.8 % intentional 62.4 % unintentional
Weng et al. [26]	Self-report	>40 % non-adherent in some form
Butler et al. [27]	Electronic monitoring	26 % missed at least 10 % of a day's medication 12 % missed at least 20 % of a day's medication
Weng et al. [28]	Electronic monitoring	26.6 % had $\leq$ 80 % of adherence
Kalil et al. [29]	Medical chart	2 %
Sketris et al. [30]	Self-report	65 %

POOR THERAPEUTIC ADHERENCE : dnDSA DEVELOPMENT



POOR THERAPEUTIC ADHERENCE : GRAFT AND PATIENT SURVIVAL DECLINE

Table 3 Final models of Cox regression containing predictors of graft loss and mortality.

	Score			χ^2	HR	95% CI for HR
	2Log likelihood					
	B	SE	95% CI			
Model for graft loss (N = 13)						
Age	−0.1*	0.05	(−0.18 to −0.1)	−4.34*	0.9	(0.82–0.99)
Sex						
Female (reference)						
Male	−3.76***	5.18	(−20.35 to −2.36)	5.07*	0.02	(0.001–6.2)
Excellent Adherence (reference)						
Good Adherence	ns					
Poor Adherence	3.88***	4.62	(1.79–15.14)	3.09	6.03	(0.46–78.55)
Model for mortality (N = 42)						
Age	ns			ns		
Sex						
Female (reference)	ns			ns		
Male						
Excellent Adherence (reference)						
Good Adherence	ns			ns		
Poor Adherence	1.28*	1.35	(1.02–3.03)	3.98*	3.07	(1.02–9.25)

* $P \leq 0.05$; ** $P \leq 0.05$; *** $P \leq 0.001$.

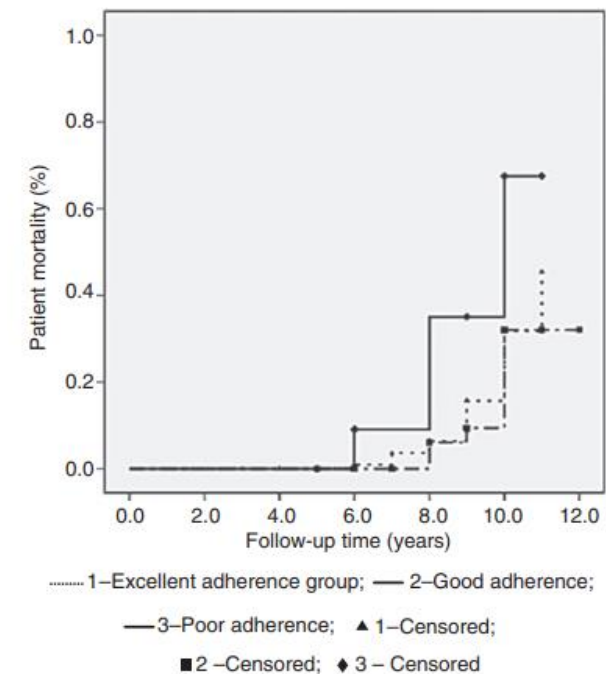


Figure 3 Kaplan-Meier Curve – Differences in patients' mortality according to patients' adherence groups. 1 – Excellent adherence group; 2 – Good adherence; 3 – Poor adherence; 1 – Censored; 2 – Censored; 3 – Censored.

POOR THERAPEUTIC ADHERENCE : PREVENTION AND SCREENING



Guideline 2.1 – KTR: Recognising non-adherence

We suggest that it is important to prevent and detect non-adherence in kidney transplant recipients. (2C)

- Factors associated with non-adherence should be identified
- An established interventional pathway should be in place for those at high risk of or with proven non-adherence
- Pathways should be in place for paediatric KTRs in transition and for adolescent KTRs

IMPROVING THERAPEUTIC ADHERENCE: STRATEGIES

Table 4 Interventions that may promote medication-taking behaviors

Interventions at the patient level	Intervention at social-economic and healthcare system level	Intervention at the therapy level
Education/cognitive interventions	Access to medication	Simplification of the regimen
Education in self-management	Assessment of social needs	Choose medication with less side effects
Education of illiterate patients	Social support	
Counseling/behavioral interventions	Nurse/pharmacist intervention protocols	
Counseling	Pharmacy-based management programs	
Follow-up and reminders		
Peer/community-based programs		
Electronic forum		
Other forms of intervention		
Reminders (e.g., short text messages)		
Electronic forums		
Electronic pill dispenser		
Medication event monitoring system		
Smartphone app		
Telecalling		

IMPROVING THERAPEUTIC ADHERENCE : BROCHURE

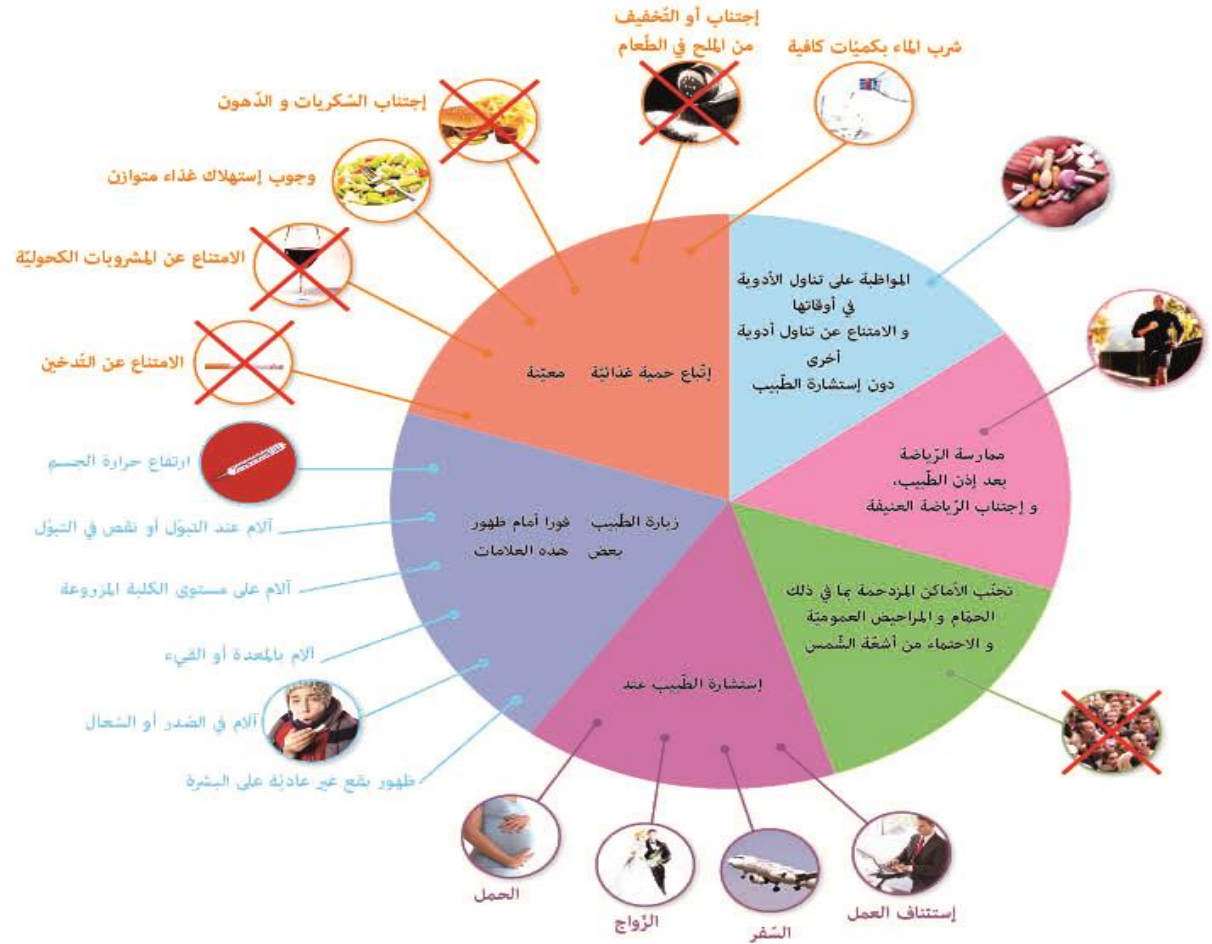
ما يجب أن تعرفه عن زرع الكلى



مطوية من إعداد :
علاء الدين بن سليمان : طالب بكلية الطب بتونس
أمل الخلووي : طالبة بكلية الطب بتونس

تحت إشراف :
أطباء وحدة زرع الكلى، قسم الطب الباطني أ
المستشفى الجامعي شارل نيكول تونس

5 - كيف نواصل حياة سليمة بعد عملية الزرع؟



spafin 01.09.2012



Ensemble, reurons pour un monde en meilleure santé*

قسم الطب الباطني أ - وحدة زرع الكلى
المستشفى الجامعي شارل نيكول تونس

IMPROVING THERAPEUTIC ADHERENCE : BROCHURE

1 - ما هو زرع الكلى؟

تتمثل عملية زرع الكلى في نقل كلية لفائدة مريض بالقصور الكلوي المزمن بعد أخذها من متبرع سليم أو في حالة موت دماغي.

2 - ما هو الفرق بين عملية زرع الكلى و غسيل الكلى؟

يمثل زرع الكلى العلاج الأنسب لحالات القصور الكلوي المزمن لما له من مزايا مقارنة بالغسيل الكلوي.

الغسيل الكلوي

- يقوم ببعض وظائف الكلية كالتخلص من نفايات الجسم والمحافظة على توازن الأملاح والسوائل في الجسم.
- يمكن من معالجة المضاعفات الحادة للقصور الكلوي المزمن في الحالات الاستعجالية.

زرع الكلى

- يعيد لجسم المريض وظيفة كلوية عادية و يجعله في صحة جيدة.
- يمكن المريض من استرجاع نشاطه العادي على المستوى المهني والاجتماعي.
- يقلص من المضاعفات المباشرة وغير المباشرة المرتبطة بالمرض وهو ما يوفر مبالغ مالية هائلة بالنسبة للمجموعة الوطنية.

- لا يعوض الوظيفة الكلوية العادية.
- يؤثر على الحالة العامة للمريض أي الشعور بالتعب ونقص في الشهية والوزن والتشاق.
- يتسبب على المدى المتوسط في ظهور مضاعفات غرس العديد من الوظائف والأعضاء وخصوصا القلب والشرايين.
- يستوجب اتباع حمية غذائية لتلافي العديد من المضاعفات التي قد تكون خطيرة.
- يؤثر سلبا على الالتزامات العائلية والمهنية للمريض لما يستوجب من تقيد بأوقات الحضر الدورية.
- يكلف المريض والمجموعة الوطنية أموالا طائلة تزداد مع الوقت.

- يستوجب القيام بعملية جراحية.
- يلزم المريض المواظبة على استعمال الأدوية المخصصة للتعويض لفقد الوفاة من رفض الجسم للكلية المزروعة.
- يتطلب مراقبة طبية دورية لاستقصاء وعلاج المضاعفات الطارئة في الأثنى هما في ذلك العوارض الجانبية التي قد تحدث جزاء استعمال بعض الادوية.

3 - من يمكنه التبرع بالكلية؟

- التبرع عمل نبيل يجب أن يتم دون أي ضغوطات.
- يشترط تطابق في الرزمة الدموية للمريض والمتبرع.

المتبرع				
أ	ب	أب	أ	ب
✓	✗	✗	✓	✗
✓	✗	✓	✗	✓
✓	✓	✓	✓	✓
✓	✗	✗	✗	✓

- هناك نوعان من المتبرعين:

أ- المتبرع الحي:

يشترط أن يكون المتبرع الحي سليما و معافى من العديد من الأمراض و خاصة منها الأمراض المعدية و الخبيثة، وأن يتمتع بكامل مداركه العقلية.

و من المستحسن أن يكون المتبرع من العائلة المقربة و ذلك لضمان التوافق مع المنتفع:



- الأب و الأم
- الأبناء و الإخوة
- الزوج و الزوجة
- العم(ة) و الخال(ة)
- الجد و الجدة

ب- المتبرع في حالة موت دماغي:

لا يمكن أخذ الأعضاء إلا بعد موافقة العائلة أو المريض نفسه قبل وفاته.

4 - ما هي فوائد زرع كلية من متبرع حي مقارنة بالمتبرع المتوفى؟

تمكن عملية زرع كلية من متبرع حي من:

- تقليص فترة انتظار الزرع

و مدة تصفية الدم حيث أن الحصول على كلية من متبرع متوفى يوجب الإنتظار لمدة طويلة، و يمكن أن يتسبب هذا في حالة من الإحباط بفقدان الأمل في العلاج إضافة إلى إمكانية حدوث بعض المضاعفات.



- برمجة موعد زرع الكلية و هو ما يمكن من التحضير الجيد للعملية بعيدا عن سياق الطوارئ.

- استعادة سريعة لوظيفتها حيث أن زرع الكلية يتم مباشرة بعد أخذها من المتبرع.

- منح المتبرع اعتزازا بالنفس و الفخر بالعمل النبيل الذي قام به و توطيد العلاقة بينه و بين المريض.

- تحسن معدل أمل الحياة عند المتبرع وذلك لتمتعه بمراقبة طبية دورية و متواصلة تمكن من تقضي الأمراض و تشخيصها و مداواتها مبكرا.



3- PREVENTION AND SCREENING OF COMPLICATIONS

A- METABOLIC COMPLICATIONS : NODAT

NODAT :

SCREENING, DIAGNOSIS AND FOLLOW-UP

Guideline 6.3 – KTR: Diabetes mellitus

We suggest that the detection and treatment of diabetes should consider:

- Screening for the development of post-transplant diabetes mellitus (PTDM) by dipstick urinalysis and measurement of blood sugar level at each clinic visit (2C)
- The diagnosis of PTDM is made based on WHO criteria for the diagnosis of diabetes mellitus based on fasting or random blood, serum glycated haemoglobin (HBA1c) or oral glucose tolerance testing (1C)
- KTR with diabetes (either prior to transplantation or PTDM) should undergo screening for diabetic complications (retinal screening, foot care, neuropathy) in line with guidelines for non KTR patients with diabetes (2D)

B- INFECTIOUS COMPLICATIONS : BK VIRUS NEPHROPATHY

BANFF 2019 :

“IF/TA” → “PVN”

TABLE 4 Updates of 2019 Banff classification for ABMR, borderline changes, TCMR, and polyomavirus nephropathy. All updates in boldface type^a

Category 1: Normal biopsy or nonspecific changes

Category 2: Antibody-mediated changes

Category 3: Borderline (Suspicious) for acute TCMR

Category 4: TCMR

Category 5: polyomavirus nephropathy^f

PVN Class 1

pvl 1 and ci 0-1

PVN Class 2

pvl 1 and ci 2-3 OR

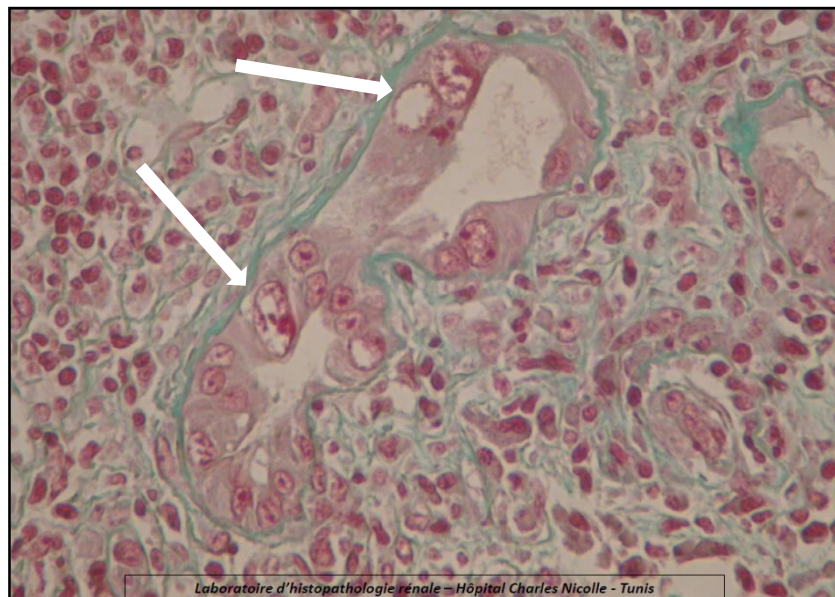
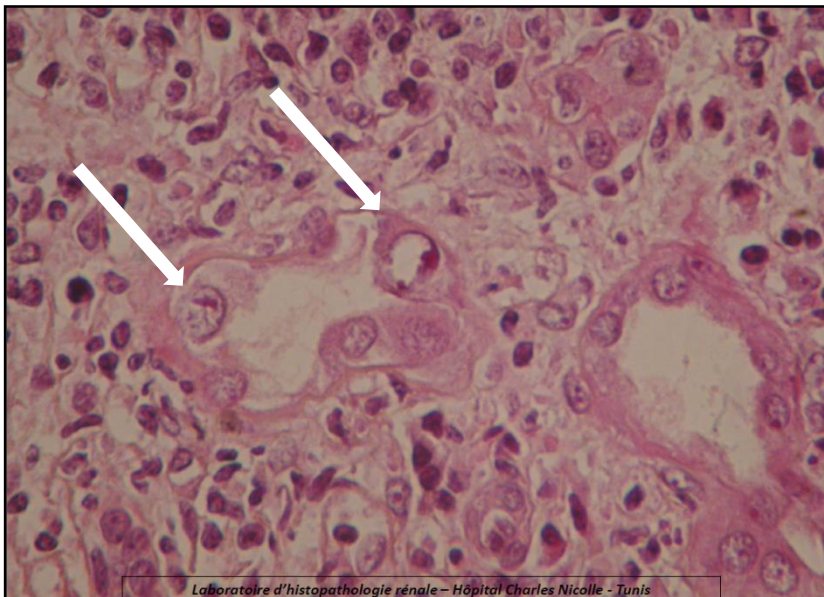
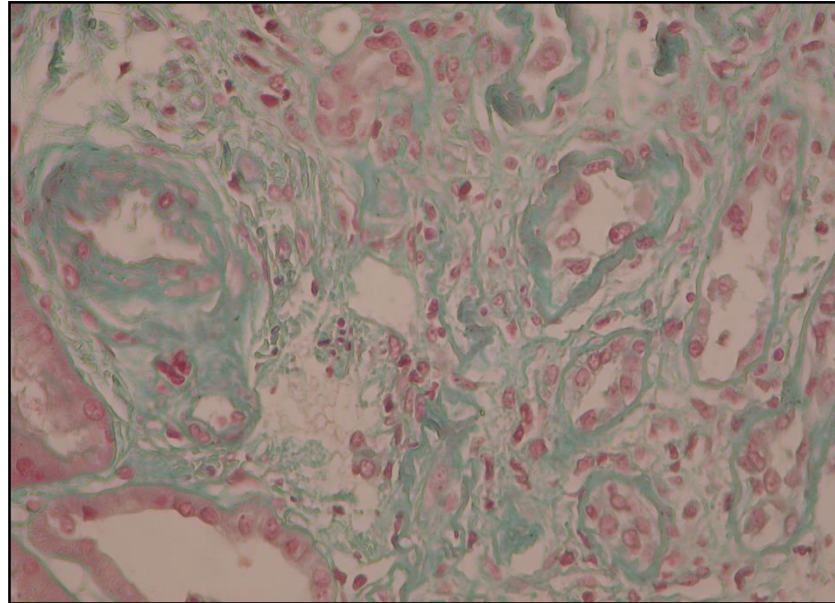
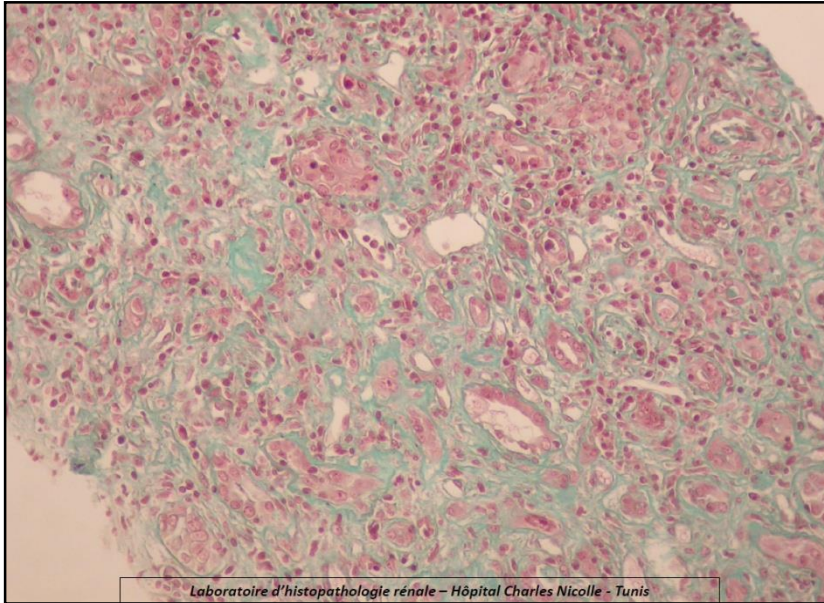
pvl 2 and ci 0-3 OR

pvl 3 and ci 0-1

PVN Class 3

pvl 3 and ci 2-3

BK VIRUS NEPHROPATHY



BK VIRUS NEPHROPATHY : SCREENING AND DIAGNOSIS

Guideline 8.6.2 – KTR: BK nephropathy

We suggest:

- Screening should also be carried out when renal function deteriorates in an unexplained fashion (2D)
- KTRs should be screened for BKV viral load or by performing urine microscopy for decoy cells or by polymerase chain reaction (PCR) on urine or serum (2C)
- Suspected BK nephropathy should be confirmed by renal biopsy, which should be stained for SV40. Two cores containing medullary tissue should ideally be examined (2D)

BK VIRUS NEPHROPATHY : SCREENING AND DIAGNOSIS

Open Journal of Organ Transplant Surgery, 2012, 2, 56-61

doi:10.4236/ojots.2012.24014 Published Online November 2012 (<http://www.SciRP.org/journal/ojots>)



The Monitoring Interest of BK Virus Load in Renal Allograft Tunisian Recipients: Prospective Study

**Yousr Gorgi¹, Mohamed M. Bacha^{1,2}, Imen Sfar¹, A. Ben Mohamed¹, Hajer Aounallah-Skhiri³,
Tarak Dhaouadi¹, Rafika Bardi¹, N. Skouri¹, Ezzeddine Abderrahim², M. Makhlouf¹,
T. Ben Romdhane¹, S. Jendoubi-Ayed¹, K. Ayed¹, Taieb Ben Abdallah¹**

BK VIRUS NEPHROPATHY : SCREENING AND DIAGNOSIS

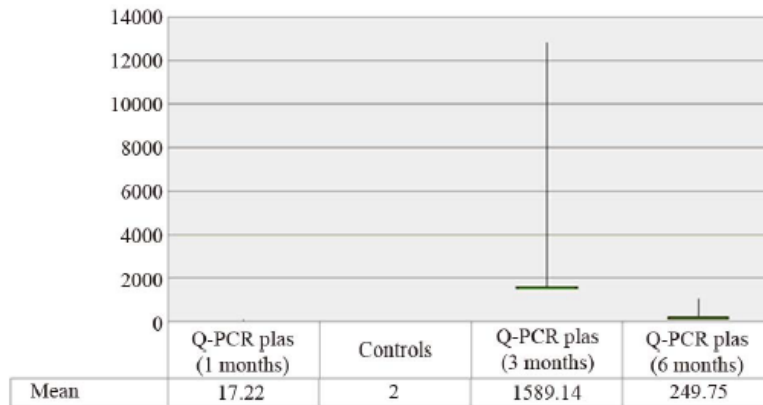


Figure 1. Distribution average values of viremia (copies/ml) in patients and controls.

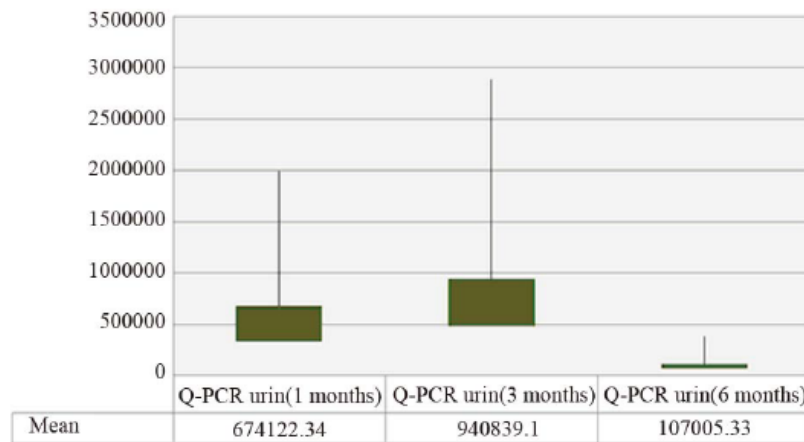
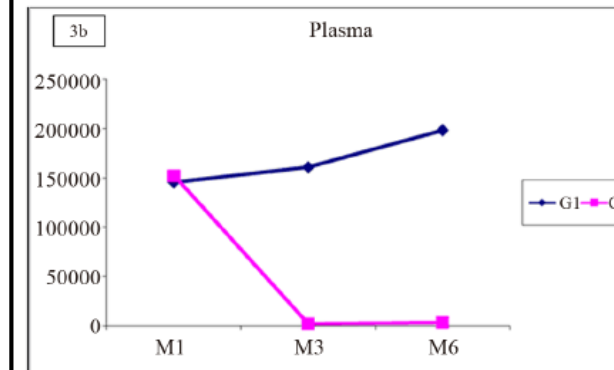
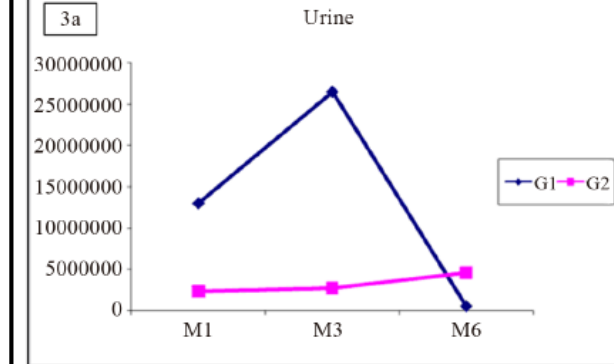


Figure 2. Distribution average values of viruria (copies/ml) in patients.



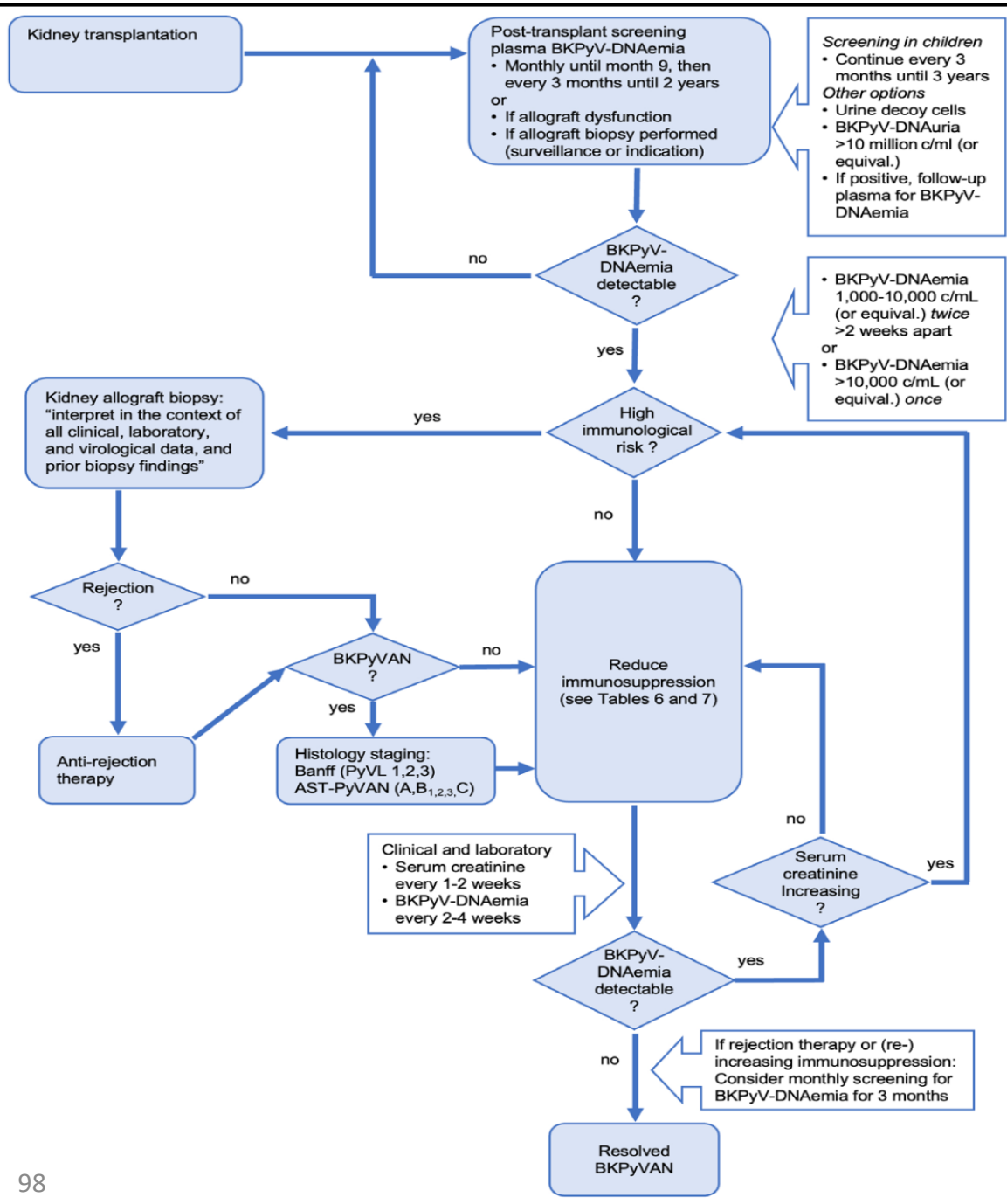
		1st Month	3rd Month	6th Month
Urine	G1	12,975,019	26,477,091	532176.91
	G2	2,285,483	2,704,945	4,585,313
Plasma	G1	145744.37	161,115	198714.75
	G2	152,506	2314	3479

Figure 3. Distribution of mean values of viruria and viremia in G1 and G2.



The Second International Consensus Guidelines on the Management of BK Polyomavirus in Kidney Transplantation

Camille N. Kotton, MD,¹ Nassim Kamar, MD, PhD,² David Wojciechowski, MD,³ Michael Eder, MD,⁴ Helmut Hopfer, MD,⁵ Parmjeet Randhawa, MD,⁶ Martina Sester, PhD,⁷ Patrizia Comoli, MD,⁸ Helio Tedesco Silva, MD, PhD,⁹ Greg Knoll, MD,¹⁰ Daniel C. Brennan, MD,¹¹ Jennifer Trofe-Clark, PharmD,^{12,13} Lars Pape, MD, PhD,¹⁴ David Axelrod, MD, MBA,¹⁵ Bryce Kiberd, MD,¹⁶ Germaine Wong, MBBS, MMed, PhD,^{17,18,19} and Hans H. Hirsch, MD^{20,21}; on behalf of The Transplantation Society International BK Polyomavirus Consensus Group*



BK VIRUS REPLICATION IN KT RECIPIENTS : SCREENING, DIAGNOSIS AND MANAGEMENT

C- NEOPLASTIC COMPLICATIONS : CANCERS AND PTLD

RISK OF MALIGNANCIES (PTLD AND KS) AFTER KT : TUNISIAN EXPERIENCE

Clin Transplant 2016; 30: 372–379 DOI: 10.1111/ctr.12694

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Clinical Transplantation

Post kidney transplantation Kaposi’s sarcoma: the experience of a Mediterranean North African center

Gorsane I, Bacha MM, Abderrahim E, Amri N, Hajri M, Ounissi M, Harzallah A, El Younsi F, Hedri H, Ben Abdallah T.



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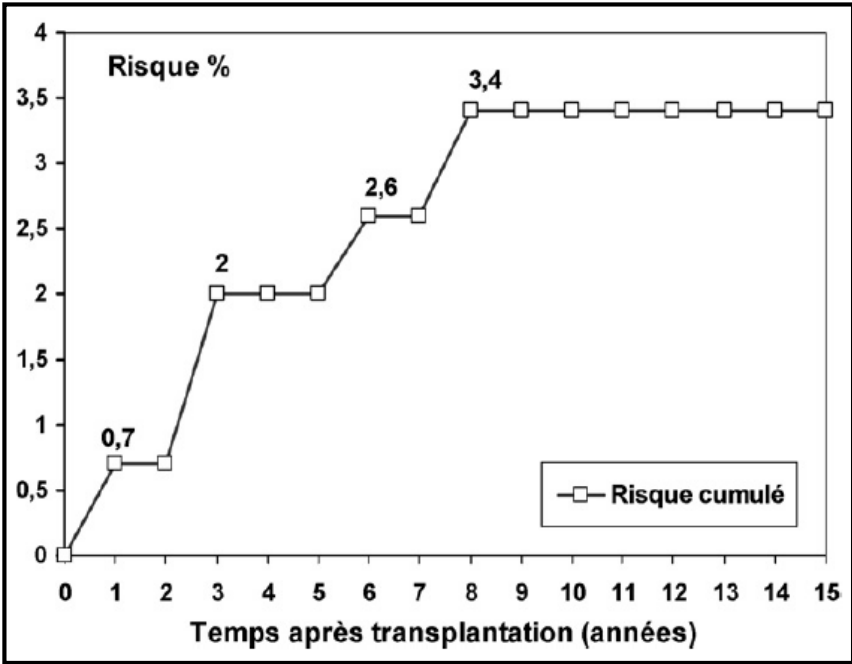
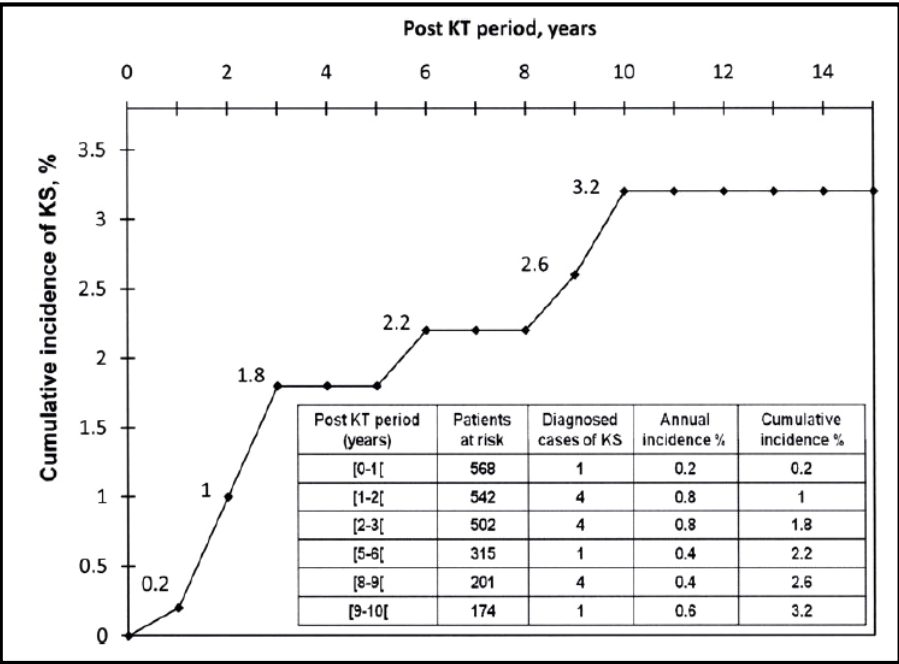
<http://france.elsevier.com/direct/REVME/>

Article original

Syndromes lymphoprolifératifs après transplantation rénale : incidence et particularités cliniques et évolutives

Lymphoproliferative disorders in kidney transplant recipients: Incidence, clinical characteristics and outcome

E. Abderrahim^{a,*}, A. Harzallah^a, S. Barbouch^a, S. Turki^a, I. Helal^a, T. Ben Abdallah^a, H. Hedri^a, F. Ben Moussa^a, R. Bardi^b, K. Ayed^b, H. Ben Maïz^a, A. Kheder^a



CANCER SCREENING AFTER KT :

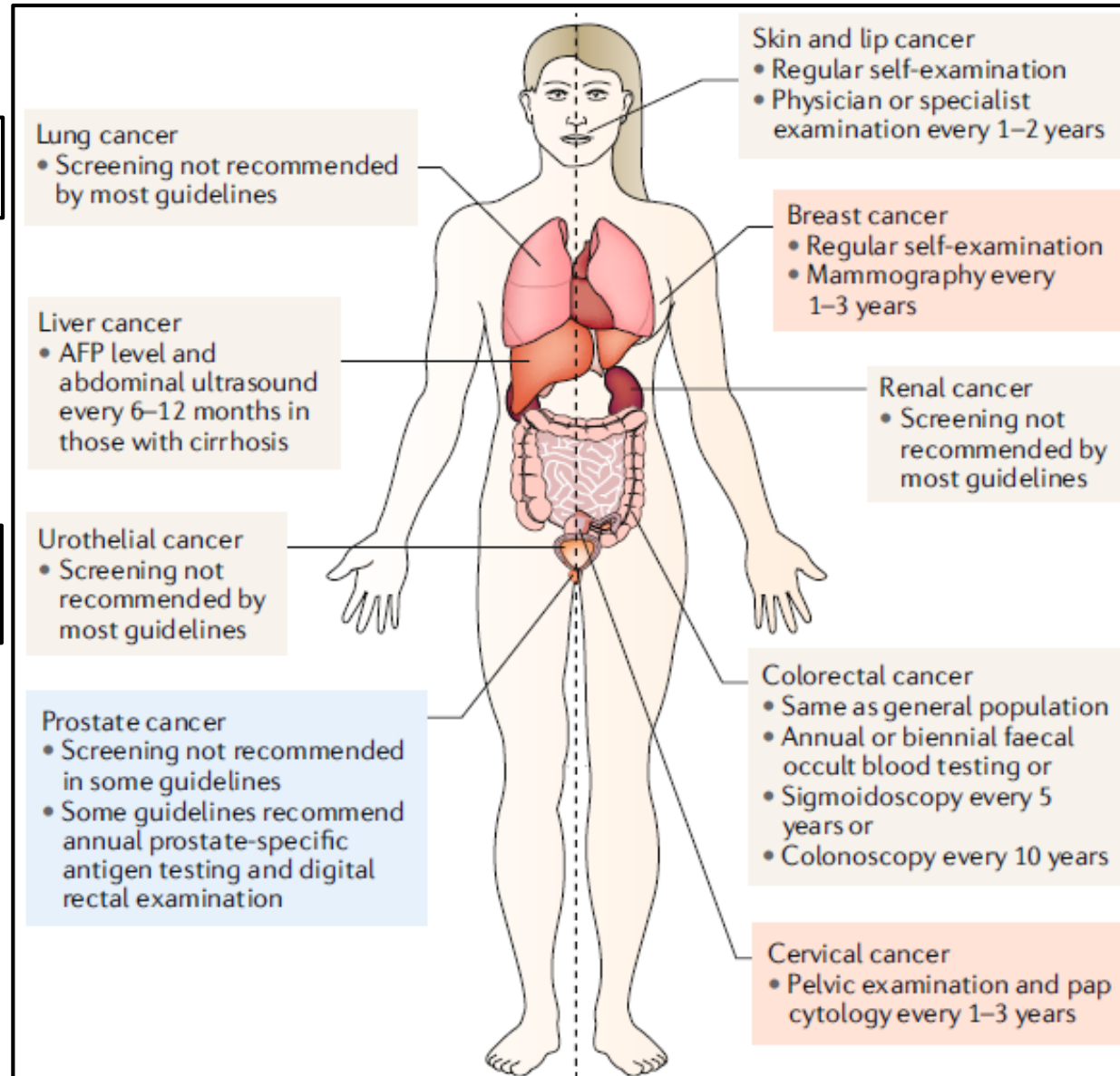
RECOMMENDATIONS



- We recommend chest CT for current or former tobacco users with a > 30 pack-year history, as per local guidelines, and chest radiograph for other KTRs (2 C).



- We strongly recommend screening for bladder carcinoma using urine cytology or cystoscopy for KTRs at increased risk, such as schistosomiasis, previous cyclophosphamide use or history of heavy smoking (>30 pack-year) (1D).



- We strongly recommend screening for RCC with US for KTRs at increased risk, such as a long time on dialysis, family history of renal cancer, acquired cystic disease, and analgesic nephropathy (1D).

4TH GCC KIDNEY TRANSPLANTATION & NEPHROLOGY CONGRESS

Follow-up Of Kidney Transplant Recipients In 2025: Towards An Individualized Approach

Mohamed Mongi BACHA

- Professor of Nephrology, Department of Internal Medicine “A”, Charles Nicolle Hospital and Faculty of Medicine of Tunis
- Vice-President of the Tunisian Society of Nephrology, Dialysis and Kidney Transplantation (STNDT)
 - Expert at the National Center for the Promotion of Organ Transplantation (CNPTO), Tunisia
 - Organization Committee Chair of the 18th AFRAN Congress, April 15-18, 2025, Tunis, Tunisia
 - Chair of the African Association of Nephrology (AFRAN) Transplant Committee

January 24, 2025

