RACCOMANDAZIONI CLINCHE SULLA VALUTAZIONE E FOLLOW-UP DEL DONATORE VIVENTE DI TRAPIANTO RENALE

S.I.T.O. – SIN

BERGAMO Spring Meeting S.I.T.O –

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Sommario

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GRUPPO SYSTEMATIC REVIEW (REVISIONE LETTERATURA PER I GRUPPI 1,2 E 3)

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BREVE PREMESSA METODOLOGICA E GUIDA ALL'INTEPRETAZIONE DEL DOCUMENTO

Score GRADE. Ciascuna raccomandazione è associata allo score GRADE che rappresenta la forza della raccomandazione e la qualità dell'evidenza che la supporta. Il GRADE è infatti uno score composto da un numero (1 o 2) e da una lettera (da A a C). Il numero si riferisce alla forza della raccomandazione, la lettera alla qualità dell'evidenza in suo supporto. La forza della raccomandazione è un giudizio che risultata dall'aver tenuto conto di tre fattori: le "utilities", cioè il beneficio percepito dal paziente, il "net benefit" cioè il beneficio clinico giudicato dal medico, ed infine i costi a carico del sistema sanitario. Il numero è "1" (in tal caso la raccomandazione comincia con "We recommend…"), quando la raccomandazione vale per pressoché la totalità dei casi, o "2", (ed in tal caso la raccomandazione comincia con "We suggest…"), quando la raccomandazione vale per la maggioranza ma non si può affermare che valga per quasi la totalità dei casi. La lettera indica invece la qualità dell'evidenza in supporto della raccomandazione: (A) alta, (B) moderata, (C) bassa, e (D) molto bassa. La lettera (A) si applica nei casi in cui l'effetto del provvedimento (oggetto della raccomandazione) è stato documentato con accuratezza: erano disponibili studi specifici sull'argomento che non avevano rilevante rischio di bias, e avevano arruolato un numero di pazienti sufficiente a fornire stime precise. La lettera (D) si applica ai casi in cui vi erano a disposizione solo studi i cui risultati apparivano assai difficili da interpretare a causa dell'elevato rischio di bias e/o della mancanza di stime sull'effetto del provvedimento. L'evidenza "A" è generalmente fornita da multipli studi clinici randomizzati (notate che gli studi randomizzati sono praticabili solo per i provvedimenti benefici e non per i fattori di rischio), oppure da meta-analysis i cui risultati appaiono di elevata qualità. Presi singolarmente, anche i migliori studi osservazionali di coorte hanno generalmente un significativo rischio di bias, per cui fornisco generalmente un'evidenza non superiore a "B". In mancanza di ottimi studi osservazionali, rimangono generalmente evidenze "C". Infine, nei casi in cui non si è ritenuto applicabile uno score GRADE, le raccomandazioni sono associate all'espressione (Not Graded).

Adozione e modifica delle raccomandazioni ERBP 2013 e KDIGO 2015. La generazione delle raccomandazioni in questo documento è stata fondata sull'adozione delle raccomandazioni ERBP 2013 e/o di quelle KDIGO (draft 2015 for public view) e sulla loro modifica. Le modifiche sono state apportata tenendo conto di vari fattori (vedi sotto), tra i quali la letteratura più recente. La ricerca della letteratura recente, e l'estrazione dei dati, è stata realizzata dal gruppo S.I.T.O. dedicato alle Systematic Review, e resa disponibile ai Gruppi di Lavoro.

Gruppi di lavoro 1, 2, e 3. I diversi argomenti sono stati ripartiti tra tre gruppi di lavoro. Ciascun gruppo di lavoro ha generato le raccomandazioni da discutere allo Spring Meeting della S.I.T.O. Nel corso nel Meeting ci sarà una sessione per ciascun gruppo di argomenti, nel corso della quale un relatore (il coordinatore del gruppo di lavoro) presenterà la proposta delle raccomandazioni, e un altro relatore (un membro del gruppo per le systematic review) presenterà la revisione della letteratura recente. Le due relazioni saranno seguite da un'ampia discussione con tutti i partecipanti.

I criteri principali per elidere parte delle raccomandazioni originarie ERBP e KDIGO sono stati l'eventuale ridondanza rispetto ad altre raccomandazioni già adottate, la inapplicabilità alla realtà Italiana, l'analisi della letteratura recente, o la non rilevanza (rispetto ai temi della valutazione di idoneità e il follow-up del donatore).

Le raccomandazioni inerenti al tema della valutazione congiunta di multipli indicatori di rischio sono state spostate e condensate nella sezione intitolata RACCOMANDAZIONI DI CARATTERE GENERALE.

1.RACCOMANDAZONI DI CARATTERE GENERALE

1. We suggest that the transplant center team should provide the donor candidate with individualized quantitative estimates of short-term and predicted lifetime incidence of ESRD risks from kidney donation, if applicable. Risks should be expressed as *absolute* rather than *relative* risks, with recognition of associated uncertainty, and in a manner that is easily understood by donor candidates. (Not Graded)

2.IPERTENSIONE

1. We recommend considering potential donors with a blood pressure <140/90 mmHg on at least three occasions without antihypertensive medication, as normotensive. (1C)

2. We suggest ambulatory blood pressure monitoring (ABPM) in potential donors who have office hypertension (blood pressure ≥140/90 mmHg) or who are taking pharmacological treatment for hypertension. (2C)

3. We suggest that, in white men and women aged above 35, well-controlled primary hypertension, as assessed by ambulatory blood pressure <130/85 mmHg, under treatment with maximum two anti-hypertensive drugs (diuretics included) is not considered a contraindication to living kidney donation. (2C)

4. We suggest to consider black race, and young age (eg ≤35years) as additional risk factors in donor candidates with well-controlled hypertension (2C)

5. We recommend discouraging hypertensive donors with evidence of target organ damage such as left ventricular hypertrophy, hypertensive retinopathy and micro-albuminuria. (1C)

6. We suggest that these potential donors could be re-evaluated for disappearance of this target organ damage after appropriate treatment. (2D)

3.OBESITÀ

1. We suggest a BMI >40 kg/m2 is a contraindication to donation. (2C)

2. We suggest that the decision to approve donation in candidates with obesity defined by BMI ≥ 30 to 40 kg/m2 should be individualized based in part on the predicted lifetime incidence of ESRD (2C)

3. We suggest that candidate donors with BMI between 30 and 40 should be enrolled in a predonation weight loss programme (2B)

4. We suggest to assess the stability of recent weight loss over one to several months prior to donation. We suggest that the period of assessment could be extended to over 12 months after bariatric surgery (Not Graded)

5. We recommend counseling obese and overweight donors for weight loss also after donation (1B)

6. We recommend that donor candidates with a prior history of bariatric surgery known to carry increased risk of developing nephrocalcinosis and kidney stones (e.g. jejunoileal bypass) should be assessed by renal imaging and 24hr urine oxalate excretion and calcium-oxalate relative supersaturation, and other urinary risk factors for kidney stones. Those with abnormal findings should be excluded from donation (1C)

4.DIABETE E IPERLIPEMA

1. We recommend prior diagnosis of diabetes mellitus, history of gestational diabetes, and family history of diabetes should be assessed during the donor candidate evaluation. *(Not Graded)*

2. We recommend glycemia should be assessed by fasting blood glucose and/or glycated hemoglobin (% HbA1c) prior to donation. *(Not Graded)*

3. We recommend 2-hour glucose tolerance testing should be performed in donor candidates with elevated fasting blood glucose, history of gestational diabetes, or family history of diabetes in a first-degree relative, and results be used to classify *(Not Graded)*

4. We recommend diabetes mellitus is a contraindication to donation, other than in exceptional circumstances. (1D)

5. We suggest impaired glucose tolerance is not a contraindication to donation: donor candidates with impaired glucose tolerance should be counseled regarding their increased lifetime risk for progression to diabetes and subsequent end-organ complications, and the importance of healthy lifestyle behaviors to reduce risks. Those who are approved to donate should be counseled on lifestyle interventions, including healthy diet, regular exercise, weight loss and on the importance of regular medical follow-up after donation. *(Not Graded)* (2C)

6. We suggest fasting lipid profile (including total cholesterol, LDL, HDL and triglycerides) should be measured prior to donation as part of an overall cardiovascular risk assessment. *(Not Graded)*

7. We suggest donor candidates with severe or uncontrolled hyperlipidemias should be excluded from donation due to increased risk of premature arteriosclerotic cardiovascular disease in the general population. *(Not Graded)*

8. We suggest the decision to approve donation in persons with mild or moderate dyslipidemia should be individualized based on their predicted lifetime incidence of ESRD *(Not Graded)*

5.TABAGISMO

1. We suggest present and past use of other tobacco products should be assessed during the donor candidate evaluation. (Not Graded)

2. We suggest donor candidates who use tobacco products should be advised of the risks of perioperative complications, cancer, cardio-pulmonary disease and ESRD, and should be referred to locally available tobacco cessation support programs. (Not Graded)

3. We suggest active smokers should be encouraged to quit smoking for at least 4 weeks prior to donation surgery to decrease the risk of perioperative complications. (Not Graded)

6.CALCOLOSI

1. We suggest that all donor candidates should have a detailed personal history about any prior kidney stones, including the composition of kidney stones, the number of kidney stones, and the family history for any first degree relatives with kidney stones (Not Graded).

2. We suggest that any imaging done as part of the donor evaluation (such as CT scan) should be examined for the presence of kidney stones. (Not Graded)

3. We suggest that all donor candidates with a history of kidney stones or evidence of kidney stones on imaging, be assessed whenever possible for any underlying disease potentially causing kidney stones, and for major urinary risk factors for kidney stone formation (such as urinary volume, urine sodium, calcium, oxalate, citrate, and uric acid excretion) (Not Graded)

4. We suggest that a decision to proceed with donation in a candidate with prior or current kidney stones should be based on a risk assessment of recurrence. (Not Graded)

5. We suggest that donors affected by significant bilateral kidney stones should be excluded from donation (1C).

6. We recommend that the donor be left with no significant stone in their remaining kidney. (1C)

7. We suggest that donor candidates with current or prior evidence of kidney stones should be encouraged to follow evidence-based dietary recommendations for the general population (increased fluid intake, low animal protein, low sodium intake), or undergo evidence-based drug treatment whenever indicated (use of thiazides, citrates, allopurinol) to minimize the risk of stone recurrence after donation (2B)

7.FUNZIONE RENALE

1. We recommend that all potential living kidney donors have their GFR assessed and that kidney function is expressed as glomerular filtration rate (GFR) and NOT as serum creatinine concentration (1A).

2. We recommend expressing GFR in mL/min/1.73 m^2 rather than mL/min. (1B)

3. We recommend that eGFR should be computed using the 2009 CKD-EPI creatinine equation or other equations that are more accurate than the 2009 CKD-EPI equation. (1B)

4. We recommend that in cases where more exact knowledge on GFR is needed or where is doubt regarding the accuracy of GFR from estimation methods (see Table), a direct measurement of GFR is undertaken by exogenous clearance methods. (1B)

5. We suggest that measurement of GFR by exogenous clearance methods should be carried out using one or more of the following methods: urinary or plasma clearance of 51Cr-EDTA, urinary or plasma clearance of iohexol, urinary or plasma clearance of inulin, and urinary clearance of 99mTc-DTPA are preferred; Other methods, including imaging, are less accurate (2C).

6. We suggest that measured creatinine clearance (mClcr) should be used if mGFR is not available (2D)

7. We recommend that donor candidates with mGFR <60 ml/min/1.73m2 should be excluded from donation. (1C)

8. We suggest that the decision to approve donor candidates with mGFR 60-89 ml/min/1.73m2 should be individualized based on the predicted lifetime incidence of ESRD, and on other donor characteristics such as young age, ethnicity, family history of renal disease, which might be associated with increased uncertainty of the estimates of lifetime incidence of ESRD (2C)

9. We suggest that mGFR ≥ 90 mL/min/ 1.73m2 should be considered as an acceptable level of kidney function for kidney donation. (2C)

10. We suggest to assess individual kidney GFR by using radionuclides or contrast agents that are excreted by glomerular filtration (e.g., 99mTc-DTPA *if* there is evidence of greater than expected asymmetry of kidney size on medical imaging,). (Not Graded)

11. We suggest that if the donor candidate's mGFR is acceptable but there is a difference in size or function between the two kidneys that is greater than expected, the transplant center should consider procuring the kidney with smaller size or lower function and leaving the donor with the kidney with larger size or higher function. (Not Graded)

8.ETÀ

1. We recommend that old age in itself is not a contraindication to donation. (1B)

2. We suggest to inform all potential young donors (e.g. aged <35) that their lifetime risk of ESRD may be difficult to assess on the basis of the current screening protocols, especially in those having first-degree relatives with ESRD, and in blacks. (Not Graded)

9.EMATURIA

1. We recommend that all donor candidates be screened for the presence of microscopic hematuria (1B)

2. We recommend that when the cause of hematuria remains uncertain despite a complete diagnostic work-up, donor renal biopsy could be considered to identify donor candidates with hematuria caused by glomerular disease (Not Graded)

3. We suggest that glomerular hematuria is a contraindication to donation. However, we recognize that thin basement membrane disease may not regarded as an absolute contraindication to donation. (Nor Graded)

10.PROTEINURIA E ALBUMINURIA

1. We recommend quantifying urinary protein excretion in all potential living donors. (1B)

2. We suggest that the final assessment of albuminuria and total proteinuria should be based on excretion rate in a timed urine specimen, rather than on random urine single time point collection (Not Graded)

3. We recommend overt albuminuria or proteinuria is a contraindication for living donation [24-h urinary albumin or total protein excretion rate >300 mg]. (1C)

4. We suggest that risk stratification of candidate donors with 24-h urinary albumin or total protein excretion rate ≤300 mg is based on albuminuria and not as total urine protein (2B)

5. We suggest that donor candidates with AER >100 mg/24h should be excluded for donation. (Not Graded)

6. We suggest that donor candidates with AER 30-100 mg/24h should be only accepted on a case by case basis (Not Graded).

7. We suggest considering AER <30 mg/24h an acceptable level for kidney donation. (Not Graded).

8. We suggest that donor renal biopsy might be considered to evaluate candidate donors with borderline-level albuminuria and no additional risk factors for donation (Not Graded).

11.RACCOMANDAZIONI FOLLOW-UP

1. We recommend that after nephrectomy, the donor is considered to be at increased lifetime risk of ESRD, compared with non-donors with the same health state. (Not Graded)

2. We recommend that, both before and after a donation, every donor should be educated about the importance of a strict post-donation clinical follow-up in order to identify, at an early stage, donors developing albuminuria, urinary abnormalities, GFR decline, or risk factors for future renal disease (such as diabetes, obesity, or hypertension) (Not Graded).

3. We recommend that blood pressure be measured annually for each donor (Not Graded)

4. We recommend that living kidney donors be monitored for long term for CKD. eGFR based on serum creatinine and urine albumin testing are particularly important parameters to follow annually in kidney donors due to concerns for the impact of donation on long-term risk for development of CKD. Assessment should include not only the absolute level of eGFR but also its trajectory over time. (Not Graded)

5. We recommend that a renal ultrasound should be performed annually during follow-up (Not graded)

6. We suggest that metabolic risk factors and unhealthy lifestyle behaviors should be identified according to guidelines for the general population (Not Graded).

7. We suggest that living donors follow up information should be reported to a national registry in order to acquire more data about long term donor safety and to increase transparency of information provided to new potential donors (Not graded)

12.GRAVIDANZA

1. We recommend that all women should be asked about their future childbearing interest and potential, as this information has implications for counselling and the need to rule out pregnancy at the time of donor nephrectomy. (Not Graded)

2. We suggest that a transplant center should not preclude a motivated, well-informed donor candidate from donation simply on the basis of her desire to have children after donation. (Not Graded)

3. We recommend informing women of childbearing age that as they are a selected from a very healthy subpopulation, donation increases their individual risk of gestational hypertension and preeclampsia from below that of the general population, to that of the general population. (1B)

4. We recommend that a woman should never donate during gestation. A woman with childbearing potential should be told about the need for contraception or abstinence from the time she is approved for donation, to the time she has recovered after her nephrectomy. The absence of pregnancy should be confirmed by a β-hCG quantitative pregnancy test immediately before donation. (Not Graded)

5. We suggest that a donor candidate with a prior history of hypertension during pregnancy (which includes preeclampsia) may be acceptable for donation, provided a transplant center after reviewing the nature of this hypertension and her other characteristics, believe the candidate's post-donation long-term risk of ESRD is low (Not Graded)