

## **Glomerular dysfunction**

### **General recommendation**

CAYA cancer survivors and their healthcare providers should be aware of the risk of a decreased GFR and proteinuria after treatment with:

- Ifosfamide (high-quality evidence for decreased GFR and proteinuria)
- Cisplatin (high-quality evidence for decreased GFR)
- Carboplatin (moderate-quality evidence for decreased GFR)
- Radiotherapy exposing the kidney (high-quality evidence for decreased GFR), including TBI (moderate-quality evidence for decreased GFR and proteinuria)
- Nephrectomy (high-quality evidence for decreased GFR)

Other risk factors for a decreased GFR and proteinuria in CAYA cancer survivors include:

- Hypertension (moderate-quality evidence for decreased GFR and proteinuria)  
(strong recommendation)

### **Who needs surveillance for glomerular dysfunction?**

GFR surveillance is recommended for CAYA cancer survivors treated with:

- Ifosfamide (high-quality evidence)
- Cisplatin (high-quality evidence)
- Radiotherapy exposing the kidney (high-quality evidence), including TBI (moderate-quality evidence)
- Nephrectomy (high-quality evidence)  
(strong recommendation)

GFR surveillance is reasonable for CAYA cancer survivors treated with carboplatin (moderate-quality evidence, moderate recommendation).

Proteinuria surveillance is recommended for CAYA cancer survivors treated with ifosfamide (high-quality evidence, strong recommendation).

Proteinuria surveillance is reasonable for CAYA cancer survivors treated with radiotherapy exposing the kidney (very low-quality evidence), including TBI (moderate-quality evidence, moderate recommendation).

### **When should surveillance be initiated and at what frequency should it be performed?**

Surveillance for glomerular dysfunction is recommended at entry into long-term follow-up and should be repeated at least every 2-5 years (expert opinion, strong recommendation).

### **What surveillance modality should be used?**

Initial screening using a creatinine-based estimating glomerular filtration rate (eGFR<sub>creat</sub>) is recommended in at-risk CAYA cancer survivors. If cystatin C is available, using a creatinine- and cystatin C based GFR estimating equation (eGFR<sub>creat-cys</sub>) is recommended (evidence-based guidelines, strong recommendation).

The use of a creatinine and cystatin C based GFR estimating equation (eGFR<sub>creat-cys</sub>) is recommended in at-risk CAYA cancer survivors in clinical settings\* when creatinine-based estimated GFR (eGFR<sub>creat</sub>) is less accurate and GFR affects clinical decision-making (evidence-based guidelines, strong recommendation).

Albumin-to-creatinine ratio or protein-to-creatinine ratio (depending on local institutional preferences) from an early morning urine sample is recommended for surveillance of proteinuria in at-risk CAYA cancer survivors (evidence-based guidelines, strong recommendation).

Note: a urine dipstick test for surveillance of proteinuria cannot be used reliably in isolation in CAYA cancer survivors (evidence-based guidelines, strong recommendation).

Blood pressure measurement should be performed yearly for CAYA cancer survivors at risk for nephrotoxicity (moderate-quality evidence, strong recommendation)

**What should be done when abnormalities are identified?**

Confirmation of an albumin-to-creatinine ratio  $\geq 3$  mg/mmol ( $\geq 30$  mg/g) with an early morning urine sample is recommended (evidence-based guidelines, strong recommendation).

Confirmation of a decreased GFR ( $< 90$  ml/min/1.73m<sup>2</sup>) after  $\geq 3$  months and ensuring adequate rehydration is recommended (evidence-based guidelines, strong recommendation).

In CAYA cancer survivors with a confirmed GFR  $< 60$  ml/min/1.73m<sup>2</sup> or albumin-to-creatinine ratio  $> 30$  mg/mmol ( $> 300$  mg/g) referral to (or consultation with) a nephrologist is recommended for further (kidney function) evaluation, interpretation of laboratory findings, potential treatment, and follow-up (evidence-based guidelines, strong recommendation).

In CAYA cancer survivors who have a albumin-to-creatinine ratio  $> 3$  mg/mmol ( $> 30$  mg/g) or survivors below the age of 40 years who have a GFR  $< 75$  ml/min/1.73m<sup>2</sup> referral to (or consultation with) a nephrologist is reasonable (depending on local practice) for further (kidney function) evaluation, interpretation of laboratory findings, potential treatment, and follow-up (expert opinion, moderate recommendation).

**What other advice should be given to at-risk CAYA cancer survivors?**

Counselling regarding lifestyle habits that are important to maintain or improve kidney health is recommended for all at risk CAYA cancer survivors, regardless of kidney function (expert opinion, strong recommendation):

- Education about caution in the use of nephrotoxic medication (e.g., NSAIDs)
- Education about the importance of hydration and caution about salt and protein intake
- Seek prompt medical attention with symptoms of a urinary tract infection

(strong recommendation)

\* Clinical settings include body habitus and changes in muscle mass (i.e. eating disorders, extreme sport, body builder, above-knee amputation, spinal cord injury with paraplegia/paraparesis or quadriplegia/quadruparesis, class III obesity), lifestyle (smoking), diet (i.e. low-protein diet, keto diets, vegetarian, high-protein diets and creatine supplement), illness other than CKD (i.e. malnutrition, cancer, heart failure, cirrhosis, catabolic consuming diseases, muscle wasting diseases), medication effects (i.e. steroids, decreases in tubular secretion, broad spectrum antibiotics that decrease extrarenal elimination).

## **Tubular dysfunction**

<b>General recommendation</b>
CAYA cancer survivors and their healthcare providers should be aware of the risk of tubular dysfunction after treatment with: <ul style="list-style-type: none"><li>• Ifosfamide (high-quality evidence for tubular dysfunction)</li><li>• Cisplatin (moderate-quality evidence for tubular dysfunction)</li></ul> (strong recommendation)
<b>Who needs surveillance for tubular dysfunction?</b>
Surveillance for tubular function is recommended for CAYA cancer survivors treated with ifosfamide (high-quality evidence, strong recommendation).
Surveillance for tubular function is reasonable for CAYA cancer survivors treated with cisplatin (moderate-quality evidence, moderate recommendation).
<b>When should surveillance be initiated and at what frequency should it be performed?</b>
Surveillance for tubular dysfunction is recommended once at entry into long-term follow-up and should be repeated as clinically indicated if abnormalities are identified (expert opinion, strong recommendation).
For CAYA cancer survivors with normal tubular function at entry into long-term follow-up it is reasonable to consider no subsequent surveillance as there is no evidence for new-onset tubular dysfunction 5 years after therapy (low-quality evidence, moderate recommendation).
<b>What surveillance modality should be used?</b>
Serum electrolytes (phosphate, magnesium, potassium) and bicarbonate are recommended for surveillance of tubular dysfunction (expert opinion, strong recommendation).
<b>What should be done when abnormalities are identified?</b>
Electrolyte supplementation is recommended, as guided by serum biochemistry, in CAYA cancer survivors with electrolyte imbalance(s) (expert opinion, strong recommendation).
Referral to (or consultation with) a nephrologist should be considered for further evaluation, interpretation of laboratory findings, potential treatment, and follow-up of CAYA cancer survivors with electrolyte imbalance(s) (expert opinion, strong recommendation).

Abbreviations: CAYA, childhood adolescent and young adult; (e)GFR, (estimated) glomerular filtration rate; NSAID, non-steroidal anti-inflammatory drug; TBI, total body irradiation.

Green representing a strong recommendation to do with a low degree of uncertainty; Yellow representing a moderate recommendation representing a higher degree of uncertainty.

## **Publication**

Kooijmans ECM, Mulder RL, Marks SD, Pavasovic V, Motwani SS, Walwyn T, Larkins NG, Kruseova J, Constine LS, Wallace WH, Green DM, Bökenkamp A, van der Pal HJH, van den Heuvel-Eibrink MM, Hjorth L, Andrés-Jensen L, Bardi E, van Dalen EC, Demoer-Goldschmidt C, Beckett K, Grönroos M, Kieran K, Mironova D, Terenziani M, Veening MA, Zieg J, Onder S, Onder AM, Routh JC, Thompson J, Hudson MM, Kremer LCM, Skinner R, Ehrhardt MJ. Nephrotoxicity Surveillance for Childhood and Young Adult Survivors of Cancer: Recommendations From the International Late Effects of Childhood Cancer Guideline Harmonization Group. J Clin Oncol. 2025 Jul 20;43(21):2433-2448.