# American College of Radiology ACR Appropriateness Criteria<sup>®</sup> Staging and Follow-Up of Leukemia

Variant 1:	
------------	--

## Child. Male. Asymptomatic. Initial staging of acute lymphoblastic leukemia.

Procedure	Appropriateness Category	<b>Relative Radiation Level</b>
US scrotum	May Be Appropriate (Disagreement)	0
Radiography chest	May Be Appropriate (Disagreement)	۲
Radiography chest abdomen pelvis	Usually Not Appropriate	€€
Radiography skeletal survey	Usually Not Appropriate	€€
MRA chest abdomen pelvis with IV contrast	Usually Not Appropriate	0
MRI abdomen and pelvis with IV contrast	Usually Not Appropriate	0
MRI abdomen and pelvis without and with IV contrast	Usually Not Appropriate	0
MRI abdomen and pelvis without IV contrast	Usually Not Appropriate	0
MRI abdomen without and with IV contrast	Usually Not Appropriate	0
MRI abdomen without IV contrast	Usually Not Appropriate	0
MRI chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	0
MRI chest abdomen pelvis without IV contrast	Usually Not Appropriate	0
MRI head without and with IV contrast	Usually Not Appropriate	0
MRI head without IV contrast	Usually Not Appropriate	0
Bone scan whole body	Usually Not Appropriate	€€€€
CT abdomen and pelvis with IV contrast	Usually Not Appropriate	€€€€
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	⋧⋧⋧⋧
CT chest with IV contrast	Usually Not Appropriate	€€€€
CT chest without and with IV contrast	Usually Not Appropriate	€€€€
CT chest without IV contrast	Usually Not Appropriate	€€€€
CT head with IV contrast	Usually Not Appropriate	∞∞∞
CT head without and with IV contrast	Usually Not Appropriate	****
CT head without IV contrast	Usually Not Appropriate	∞∞∞
Nuclear medicine ventriculography	Usually Not Appropriate	₸₽₽₽₽
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	€€€€
CT chest abdomen pelvis with IV contrast	Usually Not Appropriate	◈◈♥♥♥
CT chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	
CT chest abdomen pelvis without IV contrast	Usually Not Appropriate	€€€€
CT neck and chest with IV contrast	Usually Not Appropriate	♦€€€
CT neck and chest without and with IV contrast	Usually Not Appropriate	♥♥♥♥
CT neck and chest without IV contrast	Usually Not Appropriate	∞∞∞∞

ACR Appropriateness Criteria®

FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	<b>\$\$\$\$</b>
FDG-PET/CT whole body	Usually Not Appropriate	$\textcircled{\begin{tabular}{lllllllllllllllllllllllllllllllllll$
CTA chest abdomen pelvis with IV contrast	Usually Not Appropriate	ଡ଼ଡ଼ଡ଼ଡ଼ଡ଼

Variant 2:

Procedure	Appropriateness Category	Relative Radiation Level	
Radiography chest	May Be Appropriate (Disagreement)	•	
Radiography chest abdomen pelvis	Usually Not Appropriate	♥♥♥	
Radiography skeletal survey	Usually Not Appropriate	♦♥♥	
MRA chest abdomen pelvis with IV contrast	Usually Not Appropriate	0	
MRI abdomen and pelvis with IV contrast	Usually Not Appropriate	0	
MRI abdomen and pelvis without and with IV contrast	Usually Not Appropriate	0	
MRI abdomen and pelvis without IV contrast	Usually Not Appropriate	0	
MRI abdomen without and with IV contrast	Usually Not Appropriate	0	
MRI abdomen without IV contrast	Usually Not Appropriate	0	
MRI chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	0	
MRI chest abdomen pelvis without IV contrast	Usually Not Appropriate	0	
MRI head without and with IV contrast	Usually Not Appropriate	0	
MRI head without IV contrast	Usually Not Appropriate	0	
Bone scan whole body	Usually Not Appropriate		
CT abdomen and pelvis with IV contrast	Usually Not Appropriate	***	
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	€€€€	
CT chest with IV contrast	Usually Not Appropriate	♥♥♥♥	
CT chest without and with IV contrast	Usually Not Appropriate	€€€	
CT chest without IV contrast	Usually Not Appropriate	€€€€	
CT head with IV contrast	Usually Not Appropriate	♥♥♥	
CT head without and with IV contrast	Usually Not Appropriate	$\textcircled{\begin{tabular}{lllllllllllllllllllllllllllllllllll$	
CT head without IV contrast	Usually Not Appropriate	€€	
Nuclear medicine ventriculography	Usually Not Appropriate		
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	€€€\$	
CT chest abdomen pelvis with IV contrast	Usually Not Appropriate		
CT chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	€€€\$	
CT chest abdomen pelvis without IV contrast	Usually Not Appropriate	€€€	
CT neck and chest with IV contrast	Usually Not Appropriate	♦♥♥♥	
CT neck and chest without and with IV contrast	Usually Not Appropriate	€€€	
CT neck and chest without IV contrast	Usually Not Appropriate		
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	te 😵 🛠 🛠	
FDG-PET/CT whole body	Usually Not Appropriate	***	
CTA chest abdomen pelvis with IV contrast	Usually Not Appropriate	$\mathbf{\hat{\mathbf{x}}}\mathbf{\hat{\mathbf{x}}}\mathbf{\hat{\mathbf{x}}}$	

Procedure	Appropriateness Category	<b>Relative Radiation Level</b>	
CT chest without IV contrast	May Be Appropriate (Disagreement)	€€	
Radiography chest	Usually Not Appropriate	•	
Radiography chest abdomen pelvis	Usually Not Appropriate	€€	
Radiography skeletal survey	Usually Not Appropriate	€€	
MRA chest abdomen pelvis with IV contrast	Usually Not Appropriate	0	
MRI abdomen and pelvis with IV contrast	Usually Not Appropriate	0	
MRI abdomen and pelvis without and with IV contrast	Usually Not Appropriate	0	
MRI abdomen and pelvis without IV contrast	Usually Not Appropriate	0	
MRI abdomen without and with IV contrast	Usually Not Appropriate	0	
MRI abdomen without IV contrast	Usually Not Appropriate	0	
MRI chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	0	
MRI chest abdomen pelvis without IV contrast	Usually Not Appropriate	0	
MRI head without and with IV contrast	Usually Not Appropriate	0	
MRI head without IV contrast	Usually Not Appropriate	0	
Bone scan whole body	Usually Not Appropriate	€€	
CT abdomen and pelvis with IV contrast	Usually Not Appropriate	€€€	
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	♦€€	
CT chest with IV contrast	Usually Not Appropriate	€€€	
CT chest without and with IV contrast	Usually Not Appropriate	∞∞∞	
CT head with IV contrast	Usually Not Appropriate	♥♥♥	
CT head without and with IV contrast	Usually Not Appropriate	€€€	
CT head without IV contrast	Usually Not Appropriate	♥♥♥	
Nuclear medicine ventriculography	Usually Not Appropriate	€€€	
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	€€€	
CT chest abdomen pelvis with IV contrast	Usually Not Appropriate	∞∞∞∞	
CT chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	€€€	
CT chest abdomen pelvis without IV contrast	Usually Not Appropriate	€€€€	
CT neck and chest with IV contrast	Usually Not Appropriate	♥♥♥♥	
CT neck and chest without and with IV contrast	Usually Not Appropriate		
CT neck and chest without IV contrast	Usually Not Appropriate		
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	***	
FDG-PET/CT whole body	Usually Not Appropriate	€€€	
CTA chest abdomen pelvis with IV contrast	Usually Not Appropriate	€€€	

# <u>Variant 4:</u>

# Adult. Posttherapy evaluation of acute lymphoblastic leukemia with extra medullary disease at diagnosis.

Procedure	Appropriateness Category	<b>Relative Radiation Level</b>
CT chest abdomen pelvis with IV contrast	Usually Appropriate	ଡ଼ଡ଼ଡ଼ଡ଼
FDG-PET/CT skull base to mid-thigh	Usually Appropriate	***
FDG-PET/CT whole body	Usually Appropriate	€€€€
CT head with IV contrast	May Be Appropriate (Disagreement)	♥♥♥
CT neck and chest with IV contrast	May Be Appropriate (Disagreement)	***
Radiography chest	Usually Not Appropriate	•
Radiography chest abdomen pelvis	Usually Not Appropriate	♥♥♥
Radiography skeletal survey	Usually Not Appropriate	***
MRA chest abdomen pelvis with IV contrast	Usually Not Appropriate	0
MRI abdomen and pelvis with IV contrast	Usually Not Appropriate	0
MRI abdomen and pelvis without and with IV contrast	Usually Not Appropriate	0
MRI abdomen and pelvis without IV contrast	Usually Not Appropriate	0
MRI abdomen without and with IV contrast	Usually Not Appropriate	0
MRI abdomen without IV contrast	Usually Not Appropriate	0
MRI chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	0
MRI chest abdomen pelvis without IV contrast	Usually Not Appropriate	0
MRI head without and with IV contrast	Usually Not Appropriate	0
MRI head without IV contrast	Usually Not Appropriate	0
Bone scan whole body	Usually Not Appropriate	♥♥♥
CT abdomen and pelvis with IV contrast	Usually Not Appropriate	$\textcircled{\black}{\textcircled{\black}{\textcircled{\black}{\textcircled{\black}{\textcircled{\black}{\textcircled{\black}{\hline}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}}$
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	
CT chest with IV contrast	Usually Not Appropriate	€€€
CT chest without and with IV contrast	Usually Not Appropriate	♥♥♥
CT chest without IV contrast	Usually Not Appropriate	
CT head without and with IV contrast	Usually Not Appropriate	♥♥♥
CT head without IV contrast	Usually Not Appropriate	♥♥♥
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	€€€
CT chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	€€€
CT chest abdomen pelvis without IV contrast	Usually Not Appropriate	$\textcircled{\begin{tabular}{lllllllllllllllllllllllllllllllllll$
CT neck and chest without and with IV contrast	Usually Not Appropriate	
CT neck and chest without IV contrast	Usually Not Appropriate	
CTA chest abdomen pelvis with IV contrast	Usually Not Appropriate	$\mathbf{\hat{\mathbf{x}}}$

Procedure	Appropriateness Category	<b>Relative Radiation Level</b>
FDG-PET/CT skull base to mid-thigh	Usually Appropriate	€€€
FDG-PET/CT whole body	Usually Appropriate	€€€€
Radiography chest	May Be Appropriate (Disagreement)	•
CT chest with IV contrast	May Be Appropriate	€€
CT chest without IV contrast	May Be Appropriate (Disagreement)	€€
CT head without IV contrast	May Be Appropriate (Disagreement)	€€
Radiography chest abdomen pelvis	Usually Not Appropriate	€€
Radiography skeletal survey	Usually Not Appropriate	€€
MRA chest abdomen pelvis with IV contrast	Usually Not Appropriate	0
MRI abdomen and pelvis with IV contrast	Usually Not Appropriate	0
MRI abdomen and pelvis without and with IV contrast	Usually Not Appropriate	0
MRI abdomen and pelvis without IV contrast	Usually Not Appropriate	0
MRI abdomen without and with IV contrast	Usually Not Appropriate	0
MRI abdomen without IV contrast	Usually Not Appropriate	0
MRI chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	0
MRI chest abdomen pelvis without IV contrast	Usually Not Appropriate	0
MRI head without and with IV contrast	Usually Not Appropriate	О
MRI head without IV contrast	Usually Not Appropriate	0
Bone scan whole body	Usually Not Appropriate	♥♥♥
CT abdomen and pelvis with IV contrast	Usually Not Appropriate	∞∞∞
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	€€
CT chest without and with IV contrast	Usually Not Appropriate	♥♥♥
CT head with IV contrast	Usually Not Appropriate	♥♥♥
CT head without and with IV contrast	Usually Not Appropriate	€€€
Nuclear medicine ventriculography	Usually Not Appropriate	€€
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	₢₢₢₢
CT chest abdomen pelvis with IV contrast	Usually Not Appropriate	€€€
CT chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	♥♥♥♥
CT chest abdomen pelvis without IV contrast	Usually Not Appropriate	
CT neck and chest with IV contrast	Usually Not Appropriate	
CT neck and chest without and with IV contrast	Usually Not Appropriate	
CT neck and chest without IV contrast	Usually Not Appropriate	
CTA chest abdomen pelvis with IV contrast	Usually Not Appropriate	€€€€

<u>Variant 6:</u>

Procedure	Appropriateness Category	<b>Relative Radiation Level</b>
Radiography chest	Usually Not Appropriate	•
Radiography chest abdomen pelvis	Usually Not Appropriate	€€€
Radiography skeletal survey	Usually Not Appropriate	���
MRA chest abdomen pelvis with IV contrast	Usually Not Appropriate	0
MRI abdomen and pelvis with IV contrast	Usually Not Appropriate	0
MRI abdomen and pelvis without and with IV contrast	Usually Not Appropriate	0
MRI abdomen and pelvis without IV contrast	Usually Not Appropriate	0
MRI abdomen without and with IV contrast	Usually Not Appropriate	0
MRI abdomen without IV contrast	Usually Not Appropriate	0
MRI chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	0
MRI chest abdomen pelvis without IV contrast	Usually Not Appropriate	О
MRI head without and with IV contrast	Usually Not Appropriate	0
MRI head without IV contrast	Usually Not Appropriate	0
Bone scan whole body	Usually Not Appropriate	♥♥♥
CT abdomen and pelvis with IV contrast	Usually Not Appropriate	���
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	���
CT chest with IV contrast	Usually Not Appropriate	₸₽₽₽
CT chest without and with IV contrast	Usually Not Appropriate	���
CT chest without IV contrast	Usually Not Appropriate	���
CT head with IV contrast	Usually Not Appropriate	♥♥♥
CT head without and with IV contrast	Usually Not Appropriate	♥♥♥
CT head without IV contrast	Usually Not Appropriate	♥♥♥
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	€€€
CT chest abdomen pelvis with IV contrast	Usually Not Appropriate	����
CT chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	€€€
CT chest abdomen pelvis without IV contrast	Usually Not Appropriate	♥♥♥♥
CT neck and chest with IV contrast	Usually Not Appropriate	♦♥♥♥
CT neck and chest without and with IV contrast	Usually Not Appropriate	€€€
CT neck and chest without IV contrast	Usually Not Appropriate	$\textcircled{\begin{tabular}{lllllllllllllllllllllllllllllllllll$
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	♦♥♥♥
FDG-PET/CT whole body	Usually Not Appropriate	♥♥♥♥
CTA chest abdomen pelvis with IV contrast	Usually Not Appropriate	�����

Variant 7:

Procedure	Appropriateness Category	<b>Relative Radiation Level</b>	
CT chest abdomen pelvis with IV contrast	May Be Appropriate (Disagreement)	ଡ଼ଡ଼ଡ଼ଡ଼	
FDG-PET/CT skull base to mid-thigh	May Be Appropriate (Disagreement)	***	
FDG-PET/CT whole body	May Be Appropriate (Disagreement)	\$\$\$\$	
Radiography chest	Usually Not Appropriate	۲	
Radiography chest abdomen pelvis	Usually Not Appropriate	€€	
Radiography skeletal survey	Usually Not Appropriate	***	
MRA chest abdomen pelvis with IV contrast	Usually Not Appropriate	0	
MRI abdomen and pelvis with IV contrast	Usually Not Appropriate	0	
MRI abdomen and pelvis without and with IV contrast	Usually Not Appropriate	0	
MRI abdomen and pelvis without IV contrast	Usually Not Appropriate	0	
MRI abdomen without and with IV contrast	Usually Not Appropriate	0	
MRI abdomen without IV contrast	Usually Not Appropriate	0	
MRI chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	0	
MRI chest abdomen pelvis without IV contrast	Usually Not Appropriate	О	
MRI head without and with IV contrast	Usually Not Appropriate	0	
MRI head without IV contrast	Usually Not Appropriate	О	
Bone scan whole body	Usually Not Appropriate	€€€	
CT abdomen and pelvis with IV contrast	Usually Not Appropriate	���	
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	���	
CT chest with IV contrast	Usually Not Appropriate	���	
CT chest without and with IV contrast	Usually Not Appropriate	���	
CT chest without IV contrast	Usually Not Appropriate	���	
CT head with IV contrast	Usually Not Appropriate	���	
CT head without and with IV contrast	Usually Not Appropriate	♥♥♥	
CT head without IV contrast	Usually Not Appropriate	♥♥♥	
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	€€€	
CT chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	€€€	
CT chest abdomen pelvis without IV contrast	Usually Not Appropriate	***	
CT neck and chest with IV contrast	Usually Not Appropriate	$\textcircled{\begin{tabular}{lllllllllllllllllllllllllllllllllll$	
CT neck and chest without and with IV contrast	Usually Not Appropriate		
CT neck and chest without IV contrast	Usually Not Appropriate		
CTA chest abdomen pelvis with IV contrast	Usually Not Appropriate	♥♥♥♥♥	

<u>Variant 8:</u>

Procedure	Appropriateness Category	<b>Relative Radiation Level</b>
CT chest abdomen pelvis with IV contrast	Usually Appropriate	♦♥♥♥
FDG-PET/CT skull base to mid-thigh	Usually Appropriate	♦€€€
FDG-PET/CT whole body	Usually Appropriate	♥♥♥♥
Radiography chest	Usually Not Appropriate	۲
Radiography chest abdomen pelvis	Usually Not Appropriate	€€
MRA chest abdomen pelvis with IV contrast	Usually Not Appropriate	0
MRI abdomen and pelvis with IV contrast	Usually Not Appropriate	0
MRI abdomen and pelvis without and with IV contrast	Usually Not Appropriate	0
MRI abdomen and pelvis without IV contrast	Usually Not Appropriate	0
MRI abdomen without and with IV contrast	Usually Not Appropriate	0
MRI abdomen without IV contrast	Usually Not Appropriate	0
MRI chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	0
MRI chest abdomen pelvis without IV contrast	Usually Not Appropriate	0
Bone scan whole body	Usually Not Appropriate	€€€
CT abdomen and pelvis with IV contrast	Usually Not Appropriate	€€€
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	���
CT chest with IV contrast	Usually Not Appropriate	���
CT chest without and with IV contrast	Usually Not Appropriate	���
CT chest without IV contrast	Usually Not Appropriate	€€€
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	€€€
CT chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	€€\$
CT chest abdomen pelvis without IV contrast	Usually Not Appropriate	€€€
CT neck and chest with IV contrast	Usually Not Appropriate	♦♥♥♥
CT neck and chest without and with IV contrast	Usually Not Appropriate	€€€
CT neck and chest without IV contrast	Usually Not Appropriate	
Gallium scan whole body	Usually Not Appropriate	
CTA chest abdomen pelvis with IV contrast	Usually Not Appropriate	€€€€€

<u>Variant 9:</u>

Procedure	Appropriateness Category	Relative Radiation Level
CT chest abdomen pelvis with IV contrast	May Be Appropriate	***
CT chest abdomen pelvis without IV contrast	May Be Appropriate	****
US abdomen	Usually Not Appropriate	0
Radiography chest	Usually Not Appropriate	•
Radiography chest abdomen pelvis	Usually Not Appropriate	***
Radiography skeletal survey	Usually Not Appropriate	***
MRA chest abdomen pelvis with IV contrast	Usually Not Appropriate	0
MRI abdomen and pelvis with IV contrast	Usually Not Appropriate	0
MRI abdomen and pelvis without and with IV contrast	Usually Not Appropriate	0
MRI abdomen and pelvis without IV contrast	Usually Not Appropriate	0
MRI abdomen without and with IV contrast	Usually Not Appropriate	0
MRI abdomen without IV contrast	Usually Not Appropriate	0
MRI chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	0
MRI chest abdomen pelvis without IV contrast	Usually Not Appropriate	0
MRI head without and with IV contrast	Usually Not Appropriate	0
MRI head without IV contrast	Usually Not Appropriate	0
Bone scan whole body	Usually Not Appropriate	***
CT abdomen and pelvis with IV contrast	Usually Not Appropriate	•••
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	***
CT chest with IV contrast	Usually Not Appropriate	<b>\$\$</b>
CT chest without and with IV contrast	Usually Not Appropriate	•••
CT chest without IV contrast	Usually Not Appropriate	\$\$\$
CT head with IV contrast	Usually Not Appropriate	<b>\$\$</b>
CT head without and with IV contrast	Usually Not Appropriate	\$\$\$
CT head without IV contrast	Usually Not Appropriate	\$\$\$
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	♥♥♥♥
CT chest abdomen pelvis without and with IV contrast	Usually Not Appropriate	€€€
CT neck and chest with IV contrast	Usually Not Appropriate	
CT neck and chest without and with IV contrast	Usually Not Appropriate	€€€
CT neck and chest without IV contrast	Usually Not Appropriate	
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	
FDG-PET/CT whole body	Usually Not Appropriate	
CTA chest abdomen pelvis with IV contrast	Usually Not Appropriate	$\mathbf{\hat{\mathbf{x}}}\mathbf{\hat{\mathbf{x}}}\mathbf{\hat{\mathbf{x}}}\mathbf{\hat{\mathbf{x}}}$

#### STAGING AND FOLLOW-UP OF LEUKEMIA

Expert Panel on Systemic Oncology: Rustain L. Morgan, MD<sup>a</sup>; Tharakeswara Kumar Bathala, MD<sup>b</sup>; Sandeep S. Arora, MBBS<sup>c</sup>; Namrata Chandhok, MD<sup>d</sup>; Amanda S. Corey, MD<sup>e</sup>; Savita V. Dandapani, MD, PhD<sup>f</sup>; Lauren Kim, MD<sup>g</sup>; Lisa Law, MD<sup>h</sup>; Bahar Mansoori, MD<sup>i</sup>; Cara E. Morin, MD, PhD<sup>j</sup>; Andrew T. Trout, MD<sup>k</sup>; Darcy J. Wolfman, MD<sup>l</sup>; Terence Z. Wong, MD, PhD.<sup>m</sup>

#### **Summary of Literature Review**

#### Introduction/Background

Each year, there are an estimated 60,650 new cases of leukemia and an estimated 24,000 associated deaths [1]. The types of leukemia are based on the cell of origin and the rate at which it grows. Leukemia has a bimodal distribution most often occurring in children and adults  $\geq$ 55 years of age. Acute lymphoblastic leukemia (ALL) is the most common in children, whereas the most common type of leukemia in adults is chronic lymphocytic leukemia (CLL), followed closely by acute myeloid leukemia (AML) [1]. Leukemia is the ninth most common cancer in men and the 10th most common in women; however, it is the most common cancer in children, accounting for 28% of new pediatric cases [1]. Over the last 4 decades there has been a significant decrease in pediatric mortality associated with leukemia due to progress in treatment options. Currently, the 5-year survival is 84% for children and 75% for adolescents; however, leukemia remains the second leading cause of cancer deaths in both children and adolescents assigned male at birth and children and adolescents assigned female at birth <20 years of age.

Treatment options for patients with leukemia vary widely and include observation, chemotherapy, tyrosine kinase inhibitors, monoclonal antibodies, and radiation therapy. Treatments continue to develop with research currently exploring the utility of immunotherapy and chimeric antigen receptor (CAR) T-cell therapy. Because of the differences between types of leukemias and the variety of treatment options, imaging recommendations for these patients vary.

#### **Special Imaging Considerations**

For the purposes of distinguishing between CT and CT angiography (CTA), ACR Appropriateness Criteria topics use the definition in the <u>ACR–NASCI–SIR–SPR Practice Parameter for the Performance and Interpretation of Body</u> <u>Computed Tomography Angiography (CTA)</u> [2]:

"CTA uses a thin-section CT acquisition that is timed to coincide with peak arterial and/or venous enhancement, depending on the vascular structures to be analyzed. The resultant volumetric data set is interpreted using primary transverse reconstructions as well as multiplanar reformations and 3-D renderings."

All elements are essential: 1) timing, 2) reconstructions/reformats, and 3) 3-D renderings. Standard CTs with contrast also include timing issues and reconstructions/reformats. Only in CTA; however, is 3-D rendering a **required** element. This corresponds to the definitions that CMS has applied to the Current Procedural Terminology codes.

#### **Discussion of Procedures by Variant**

## Variant 1: Child. Male. Asymptomatic. Initial staging of acute lymphoblastic leukemia.

Imaging of patients with ALL can improve the detection of extramedullary disease involvement. This variant covers patients without suspected extra medullary disease. Accurately identifying areas of disease involvement allows for appropriate treatment, which can improve patient outcomes.

<sup>&</sup>lt;sup>a</sup>University of Colorado Denver Anschutz Medical Campus, Aurora, Colorado. <sup>b</sup>Panel Chair, The University of Texas MD Anderson Cancer Center, Houston, Texas. <sup>c</sup>Yale University School of Medicine, New Haven, Connecticut. <sup>d</sup>University of Miami, Miami, Florida; American Society of Hematology. <sup>e</sup>Atlanta VA Health Care System and Emory University, Atlanta, Georgia. <sup>f</sup>City of Hope, Duarte, California; Commission on Radiation Oncology. <sup>g</sup>Dana-Farber Cancer Institute/Brigham and Women's Hospital, Boston, Massachusetts. <sup>b</sup>Kaiser Permanente, Roseville, California; American Society of Clinical Oncology. <sup>i</sup>Fred Hutchinson Cancer Center University of Washington, Seattle, Washington. <sup>i</sup>Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio. <sup>k</sup>Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio; Commission on Nuclear Medicine and Molecular Imaging. <sup>I</sup>Johns Hopkins University School of Medicine, Washington, District of Columbia. <sup>m</sup>Duke University Medical Center, Durham, North Carolina; Commission on Nuclear Medicine and Molecular Imaging.

The American College of Radiology seeks and encourages collaboration with other organizations on the development of the ACR Appropriateness Criteria through representation of such organizations on expert panels. Participation on the expert panel does not necessarily imply endorsement of the final document by individual contributors or their respective organization.

Reprint requests to: publications@acr.org

## **Bone Scan Whole Body**

There is no relevant literature to support the use of whole body bone scan in the initial staging of asymptomatic male children with ALL.

## CT Abdomen and Pelvis With IV Contrast

A small trial of 25 pediatric patients found 3-D–enhanced CT reconstruction was more accurate for detecting renal involvement by ALL compared with ultrasound (US) [3]. This study found conventional criteria of renal length produces a higher false-positive rate [3].

## CT Abdomen and Pelvis Without and With IV Contrast

There is no relevant literature to support the use of CT abdomen and pelvis without and with intravenous (IV) contrast in the initial staging of asymptomatic male children with ALL.

## **CT Abdomen and Pelvis Without IV Contrast**

There is no relevant literature to support the use of CT abdomen and pelvis without IV contrast in the initial staging of asymptomatic male children with ALL.

## **CT Chest Abdomen Pelvis With IV Contrast**

There is no relevant literature to support the use of CT chest, abdomen, and pelvis with IV contrast in the initial staging of asymptomatic male children with ALL. If the patient has symptoms of suspected cases of extramedullary disease, a CT chest, abdomen, and pelvis with IV contrast is recommended by the National Comprehensive Cancer Network (NCCN) guidelines for evaluation [4].

## CT Chest Abdomen Pelvis Without and With IV Contrast

There is no relevant literature to support the use of CT chest, abdomen, and pelvis without and with IV contrast in the initial staging of asymptomatic male children with ALL.

## **CT** Chest Abdomen Pelvis Without IV Contrast

There is no relevant literature to support the use of CT chest, abdomen, and pelvis without IV contrast in the initial staging of asymptomatic male children with ALL.

## **CT Chest With IV Contrast**

There is no relevant literature to support the use of CT chest with IV contrast in the initial staging of asymptomatic male children with ALL.

## CT Chest Without and With IV Contrast

There is no relevant literature to support the use of CT chest without and with IV contrast in the initial staging of asymptomatic male children with ALL.

## **CT Chest Without IV Contrast**

There is no relevant literature to support the use of CT chest without IV contrast in the initial staging of asymptomatic male children with ALL.

## **CT Head With IV Contrast**

There is no relevant literature to support the use of CT head with IV contrast in the initial staging of asymptomatic male children with ALL. In patients with neurologic symptoms, CT with IV contrast is recommended by the NCCN guidelines [4].

## CT Head Without and With IV Contrast

There is no relevant literature to support the use of CT head without and with IV contrast in the initial staging of asymptomatic male children with ALL.

## **CT Head Without IV Contrast**

There is no relevant literature to support the use of CT head without IV contrast in the initial staging of asymptomatic male children with ALL.

## CT Neck and Chest With IV Contrast

There is no relevant literature to support the use of CT neck and chest with IV contrast in the initial staging of asymptomatic male children with ALL. If the patient has symptoms of suspected cases of extramedullary disease, a CT neck and chest with IV contrast is recommended for evaluation by the NCCN guidelines [4].

## CT Neck and Chest Without and With IV Contrast

There is no relevant literature to support the use of CT neck and chest without and with IV contrast in the initial staging of asymptomatic male children with ALL.

## CT Neck and Chest Without IV Contrast

There is no relevant literature to support the use of CT neck and chest without IV contrast in the initial staging of asymptomatic male children with ALL.

## CTA Chest Abdomen Pelvis With IV Contrast

There is no relevant literature to support the use of CTA chest, abdomen, and pelvis with IV contrast in the initial staging of asymptomatic male children with ALL.

## FDG-PET/CT Skull Base To Mid-Thigh

There is no relevant literature to support the use of fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)-PET/CT skull base to mid-thigh in the initial staging of asymptomatic male children with ALL.

## FDG-PET/CT Whole Body

There is no relevant literature to support the use of FDG-PET/CT whole body in the initial staging of asymptomatic male children with ALL. In patients with a clinical concern for acute lymphoblastic lymphoma, a whole body FDG-PET/CT is recommended by the NCCN guidelines [4].

## MRA Chest Abdomen Pelvis With IV Contrast

There is no relevant literature to support the use of MR angiography (MRA) chest, abdomen, and pelvis with IV contrast in the initial staging of asymptomatic male children with ALL.

## MRI Abdomen and Pelvis With IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis with IV contrast in the initial staging of asymptomatic male children with ALL.

## MRI Abdomen and Pelvis Without and With IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis without and with IV contrast in the initial staging of asymptomatic male children with ALL.

## **MRI Abdomen and Pelvis Without IV Contrast**

As part of the prospective, opioid analgesia for acute low back pain and neck pain (OPioids for acute SpinAL pain [OPAL] trial), MRI scans of 76 pediatric patients were reviewed for osteonecrosis before antileukemic treatment. In MRI screening, 14 osteonecrotic lesions were found in 7 patients [5]; the authors suggest the need for MRI for pretherapy screening for osteonecrosis in patients diagnosed with ALL[5].

## MRI Abdomen Without and With IV Contrast

There is no relevant literature to support the use of MRI abdomen without and with IV contrast in the initial staging of asymptomatic male children with ALL.

# MRI Abdomen Without IV Contrast

There is no relevant literature to support the use of MRI abdomen without IV contrast in the initial staging of asymptomatic male children with ALL.

## MRI Chest Abdomen Pelvis Without and With IV Contrast

There is no relevant literature to support the use of MRI chest, abdomen, and pelvis without and with IV contrast in the initial evaluation of asymptomatic male children with ALL.

## MRI Chest Abdomen Pelvis Without IV Contrast

There is no relevant literature to support the use of MRI chest, abdomen, and pelvis without IV contrast in the initial staging of asymptomatic male children with ALL.

## MRI Head Without and With IV Contrast

A prospective study of 51 patients with ALL and 30 age-matched controls found diffusion-weighted imaging (DWI) was useful for detection of skull infiltration in children with ALL, which normalizes after therapy and complete remission [6]. An additional study of 377 pediatric patients treated for ALL without irradiation found that a quarter of the patients had leukoencephalopathy during therapy. The leukoencephalopathy could involve up to 10% of the white matter and was associated with decreased neurocognitive performance [7]. However, a retrospective study of

215 pediatric patients with newly diagnosed ALL found cranial MRI did not improve the detection of central nervous system (CNS) involvement and added no value [8].

An additional international retrospective cohort study of 1,877 pediatric patients with ALL found that 3.5% (66) had CNS involvement and 45% (30/66) had CNS symptoms [9]. Of the 66 patients with CNS involvement, imaging was performed on 32, which confirmed CNS involvement in 6 of the 21 patients who were imaged and had symptoms and 5 of the 11 imaged patients who were asymptomatic. There was no overall survival difference between CNS-positive patients with or without symptoms (P = .53) [9]. The authors concluded that radiological imaging of asymptomatic children with CNS leukemia at diagnosis lacks clinical importance but may be useful in patients with cranial nerve symptoms and negative cerebrospinal fluid (CSF) analysis. In addition, the authors state imaging of symptomatic patients is indicated to exclude other causes of the underlying symptoms [9].

## MRI Head Without IV Contrast

A prospective study of 51 patients with ALL and 30 age-matched controls found DWI was useful for the detection of skull infiltration in children with ALL, which normalizes after therapy and complete remission [6]. An additional study of 377 pediatric patients treated for ALL without irradiation found that a quarter of the patients had leukoencephalopathy during therapy. The leukoencephalopathy could involve up to 10% of the white matter and was associated with decreased neurocognitive performance [7]. However, a retrospective study of 215 pediatric patients with newly diagnosed ALL found cranial MRI did not improve the detection of CNS involvement and added no value [8].

An additional international retrospective cohort study of 1,877 pediatric patients with ALL found that 3.5% (66) had CNS involvement and 45% (30/66) had CNS symptoms [9]. Of the 66 patients with CNS involvement, imaging was performed on 32, which confirmed CNS involvement in 6 of the 21 patients who were imaged and had symptoms and 5 of the 11 imaged patients who were asymptomatic. There was no overall survival difference between CNS-positive patients with or without symptoms (P = .53) [9]. The authors concluded that radiological imaging of asymptomatic children with CNS leukemia at diagnosis lacks clinical importance but may be useful in patients with cranial nerve symptoms and negative CSF analysis. In addition, the authors state the imaging of symptomatic patients is indicated to exclude other causes of the underlying symptoms [9].

## Nuclear Medicine Ventriculography

There is no relevant literature to support the use of nuclear medicine ventriculography in the initial staging of asymptomatic male children with ALL.

# **Radiography Chest**

A retrospective study of 990 patients 1 to 18 years of age with ALL found chest radiographs detected various intrathoracic lesions and was helpful in treatment planning [10]. Findings were peribronchial/perihilar thickening (n = 187 [19.0%]), pulmonary opacity/infiltrate (n = 159 [16.1%]), pleural effusion/thickening (n = 109 [11.1%]), mediastinal mass (n = 107 [10.9%]), and cardiomegaly (n = 68 [6.9%]). Patients with a mediastinal mass, pleural effusion/thickening, tracheal deviation/compression, or pulmonary opacity/infiltrate were more likely to receive less invasive sedation and more intensive care unit admissions and respiratory support ( $P \le .001$  for all). Cardiomegaly was associated with intensive care unit admission (P = .008) [10].

## **Radiography Chest Abdomen Pelvis**

There is no relevant literature to support the use of radiography chest, abdomen, and pelvis in the initial staging of asymptomatic male children with ALL.

## **Radiography Skeletal Survey**

There is no relevant literature to support the use of radiography skeletal survey in the initial staging of asymptomatic male children with ALL.

## **US Scrotum**

NCCN guidelines recommend that male pediatric patients should be evaluated for testicular involvement with a clinical examination and scrotal US in the evaluation of ALL at initial diagnosis [4].

# Variant 2: Child. Female. Asymptomatic. Initial staging of acute lymphoblastic leukemia.

Imaging of patients with ALL can improve the detection of extramedullary disease involvement. Accurately identifying areas of disease involvement allows for appropriate treatment, which can improve patient outcomes.

## **Bone Scan Whole Body**

There is no relevant literature to support the use of whole body bone scan in the initial staging of asymptomatic female children with ALL.

## CT Abdomen and Pelvis With IV Contrast

A small trial of 25 pediatric patients found 3-D-enhanced CT reconstruction was more accurate for detecting renal involvement by ALL compared with US [3]. This study found conventional criteria of renal length produces a higher false-positive rate [3].

## CT Abdomen and Pelvis Without and With IV Contrast

There is no relevant literature to support the use of CT abdomen and pelvis without and with IV contrast in the initial staging of asymptomatic female children with ALL.

## CT Abdomen and Pelvis Without IV Contrast

There is no relevant literature to support the use of CT abdomen and pelvis without and with IV contrast in the initial staging of asymptomatic female children with ALL.

## **CT** Chest Abdomen Pelvis With IV Contrast

There is no relevant literature to support the use of CT chest, abdomen, and pelvis with IV contrast in the initial staging of asymptomatic female children with ALL. If the patient has symptoms of suspected cases of extramedullary disease, a CT chest, abdomen, and pelvis with IV contrast is recommended by the NCCN guidelines for evaluation [4].

## CT Chest Abdomen Pelvis Without and With IV Contrast

There is no relevant literature to support the use of CT chest, abdomen, and pelvis without and with IV contrast in the initial staging of asymptomatic female children with ALL.

## **CT** Chest Abdomen Pelvis Without IV Contrast

There is no relevant literature to support the use of CT chest, abdomen, and pelvis without IV contrast in the initial staging of asymptomatic female children with ALL.

## **CT Chest With IV Contrast**

There is no relevant literature to support the use of CT chest with IV contrast in the initial staging of asymptomatic female children with ALL.

## CT Chest Without and With IV Contrast

There is no relevant literature to support the use of CT chest without and with IV contrast in the initial staging of asymptomatic female children with ALL.

## **CT Chest Without IV Contrast**

There is no relevant literature to support the use of CT chest without IV contrast in the initial staging of asymptomatic female children with ALL.

## **CT Head With IV Contrast**

There is no relevant literature to support the use of CT head with IV contrast in the initial staging of asymptomatic female children with ALL. In patients with neurologic symptoms, CT head with IV contrast is recommended by the NCCN guidelines [4].

## **CT Head Without and With IV Contrast**

There is no relevant literature to support the use of CT head without and with IV contrast in the initial staging of asymptomatic female children with ALL.

## **CT Head Without IV Contrast**

There is no relevant literature to support the use of CT head without IV contrast in the initial staging of ALL.

# CT Neck and Chest With IV Contrast

There is no relevant literature to support the use of CT neck and chest with IV contrast in the initial staging of asymptomatic female children with ALL. If the patient has symptoms of suspected cases of extramedullary disease, a CT neck and chest with IV contrast is recommended for evaluation [4].

## CT Neck and Chest Without and With IV Contrast

There is no relevant literature to support the use of CT neck and chest without and with IV contrast in the initial staging of asymptomatic female children with ALL.

## CT Neck and Chest Without IV Contrast

There is no relevant literature to support the use of CT neck and chest without IV contrast in the initial staging of asymptomatic female children with ALL. If the patient has symptoms of suspected cases of extramedullary disease, a CT neck and chest without IV contrast is recommended by the NCCN guidelines for the initial evaluation [4].

## **CTA Chest Abdomen Pelvis With IV Contrast**

There is no relevant literature to support the use of CTA chest, abdomen, and pelvis with IV contrast in the initial staging of asymptomatic female children with ALL.

## FDG-PET/CT Skull Base To Mid-Thigh

There is no relevant literature to support the use of FDG-PET/CT skull base to mid-thigh in the initial staging of asymptomatic female children with ALL.

## FDG-PET/CT Whole Body

There is no relevant literature to support the use of FDG-PET/CT whole body in the initial staging of asymptomatic female children with ALL. In patients with a clinical concern for acute lymphoblastic lymphoma, a whole body FDG-PET/CT is recommended by the NCCN guidelines [4].

## MRA Chest Abdomen Pelvis With IV Contrast

There is no relevant literature to support the use of MRA chest, abdomen, and pelvis with IV contrast in the initial staging of asymptomatic female children with ALL.

## MRI Abdomen and Pelvis With IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis with IV contrast in the initial staging of asymptomatic female children with ALL.

## MRI Abdomen and Pelvis Without and With IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis without and with IV contrast in the initial staging of asymptomatic female children with ALL.

## MRI Abdomen and Pelvis Without IV Contrast

As part of the prospective OPAL trial, MRI scans of 76 pediatric patients were reviewed for osteonecrosis before antileukemic treatment. In MRI screening, 14 osteonecrotic lesions were found in 7 patients [5]. The authors suggest the need for pretherapy MRI screening for osteonecrosis in patients diagnosed with ALL [5].

## MRI Abdomen Without and With IV Contrast

There is no relevant literature to support the use of MRI abdomen without and with IV contrast in the initial staging of asymptomatic female children with ALL.

# MRI Abdomen Without IV Contrast

There is no relevant literature to support the use of MRI abdomen without IV contrast in the initial staging of asymptomatic female children with ALL.

# MRI Chest Abdomen Pelvis Without and With IV Contrast

There is no relevant literature to support the use of MRI chest, abdomen, and pelvis without and with IV contrast in the initial staging of asymptomatic female children with ALL.

## MRI Chest Abdomen Pelvis Without IV Contrast

There is no relevant literature to support the use of MRI chest, abdomen, and pelvis without IV contrast in the initial staging of asymptomatic female children with ALL.

## **MRI Head Without and With IV Contrast**

A prospective study of 51 patients with ALL and 30 age-matched controls found DWI was a useful tool for the detection of skull infiltration in children with ALL, which normalizes after therapy and complete remission [6]. An additional study of 377 pediatric patients treated for ALL without irradiation found that a quarter of the patients had leukoencephalopathy during therapy. The leukoencephalopathy could involve up to 10% of the white matter and was associated with decreased neurocognitive performance [7]. However, a retrospective study of 215 pediatric

patients with newly diagnosed ALL found cranial MRI did not improve the detection of CNS involvement and added no value [8].

An additional international retrospective cohort study of 1,877 pediatric patients with ALL found 3.5% (66) had CNS involvement and 45% (30/66) had CNS symptoms [9]. Of the 66 patients with CNS involvement, imaging was performed on 32, which confirmed CNS involvement in 6 of the 21 patients who were imaged and had symptoms and 5 of the 11 imaged patients who were asymptomatic. There was no overall survival difference between CNS-positive patients with or without symptoms (P = .53) [9]. The authors concluded that radiological imaging of asymptomatic children with CNS leukemia at diagnosis lacks clinical importance but may be useful in patients with cranial nerve symptoms and negative CSF analysis. In addition, the authors state the imaging of symptomatic patients is indicated to exclude other causes of the underlying symptoms [9].

## MRI Head Without IV Contrast

A prospective study of 51 patients with ALL and 30 age-matched controls found DWI was a useful tool for the detection of skull infiltration in children with ALL, which normalizes after therapy and complete remission [6]. An additional study of 377 pediatric patients treated for ALL without irradiation found that a quarter of the patients had leukoencephalopathy during therapy. The leukoencephalopathy could involve up to 10% of the white matter and was associated with decreased neurocognitive performance [7]. However, a retrospective study of 215 pediatric patients with newly diagnosed ALL found cranial MRI did not improve the detection of CNS involvement and added no value [8].

An additional international retrospective cohort study of 1,877 pediatric patients with ALL found 3.5% (66) had CNS involvement and 45% (30/66) had CNS symptoms [9]. Of the 66 patients with CNS involvement, imaging was performed on 32, which confirmed CNS involvement in 6 of the 21 patients who were imaged and had symptoms and 5 of the 11 imaged patients who were asymptomatic. There was no overall survival difference between CNS-positive patients with or without symptoms (P = .53) [9]. The authors concluded that radiological imaging of asymptomatic children with CNS leukemia at diagnosis lacks clinical importance but may be useful in patients with cranial nerve symptoms and negative CSF analysis. In addition, the authors state the imaging of symptomatic patients is indicated to exclude other causes of the underlying symptoms [9].

## Nuclear Medicine Ventriculography

There is no relevant literature to support the use of nuclear medicine ventriculography in the initial staging of asymptomatic female children with ALL.

# **Radiography Chest**

A retrospective study of 990 patients 1 to 18 years of age with ALL found chest radiographs detected various intrathoracic lesions and was helpful in treatment planning [10]. Findings were peribronchial/perihilar thickening (n = 187 [19.0%]), pulmonary opacity/infiltrate (n = 159 [16.1%]), pleural effusion/thickening (n = 109 [11.1%]), mediastinal mass (n = 107 [10.9%]), and cardiomegaly (n = 68 [6.9%]). Patients with a mediastinal mass, pleural effusion/thickening, tracheal deviation/compression, or pulmonary opacity/infiltrate were more likely to receive less invasive sedation and more intensive care unit admissions and respiratory support ( $P \le .001$  for all). Cardiomegaly was associated with intensive care unit admission (P = .008) [10].

## **Radiography Chest Abdomen Pelvis**

There is no relevant literature to support the use of radiography chest, abdomen, and pelvis in the initial staging of asymptomatic female children with ALL.

## **Radiography Skeletal Survey**

There is no relevant literature to support the use of radiography skeletal survey in the initial staging of asymptomatic female children with ALL.

# Variant 3: Adult. Asymptomatic. Initial staging of acute lymphoblastic leukemia.

Imaging of patients with ALL can improve the detection of extramedullary disease involvement. Accurately identifying areas of disease involvement allows for appropriate treatment, which can improve patient outcomes.

# **Bone Scan Whole Body**

There is no relevant literature to support the use of whole body bone scan in the staging of asymptomatic adult patients with ALL.

## CT Abdomen and Pelvis With IV Contrast

There is no relevant literature to support the use of CT abdomen and pelvis with IV contrast in the initial staging of asymptomatic adult patients with ALL.

## CT Abdomen and Pelvis Without and With IV Contrast

There is no relevant literature to support the use of CT abdomen and pelvis without and with IV contrast in the initial staging of asymptomatic adult patients with ALL.

## CT Abdomen and Pelvis Without IV Contrast

There is no relevant literature to support the use of CT abdomen and pelvis without IV contrast in the initial staging of asymptomatic adult patients with ALL.

## **CT** Chest Abdomen Pelvis With IV Contrast

There is no relevant literature to support the use of CT chest, abdomen, and pelvis with IV contrast in the initial staging of asymptomatic adult patients with ALL.

## CT Chest Abdomen Pelvis Without and With IV Contrast

There is no relevant literature to support the use of CT chest, abdomen, and pelvis without and with IV contrast in the initial staging of asymptomatic adult patients with ALL.

## CT Chest Abdomen Pelvis Without IV Contrast

There is no relevant literature to support the use of CT chest, abdomen, and pelvis without IV contrast in the initial staging of asymptomatic adult patients with ALL.

## **CT Chest With IV Contrast**

A prospective study of 198 patients with hematologic malignancies (including ALL and AML) found presymptomatic CT chest examination identified abnormalities in 36% of patients [11]. The multivariate analysis found patients with an abnormal baseline CT chest had an adjusted hazard ratio of 1.52 (95% confidence interval [CI], 1.27-5.03) [11].

## CT Chest Without and With IV Contrast

There is no relevant literature to support the use of CT chest without and with IV contrast in the initial staging of asymptomatic adult patients with ALL.

## **CT Chest Without IV Contrast**

A prospective study of 198 patients with hematologic malignancies (including ALL and AML) found presymptomatic CT chest examination identified abnormalities in 36% of patients [11]. The multivariate analysis found patients with an abnormal baseline CT chest had an adjusted hazard ratio of 1.52 (95% CI, 1.27-5.03) [11].

## **CT Head With IV Contrast**

There is no relevant literature to support the use of CT head with IV contrast in the initial staging of asymptomatic adult patients with ALL. In patients with neurologic symptoms, CT head with IV contrast is recommended by the NCCN guidelines [4].

## CT Head Without and With IV Contrast

There is no relevant literature to support the use of CT head without and with IV contrast in the initial staging of asymptomatic adult patients with ALL.

## **CT Head Without IV Contrast**

There is no relevant literature to support the use of CT head without IV contrast in the initial staging of asymptomatic adult patients with ALL.

## CT Neck and Chest With IV Contrast

There is no relevant literature to support the use of CT neck and chest with IV contrast in the initial staging of asymptomatic adult patients with ALL.

## CT Neck and Chest Without and With IV Contrast

There is no relevant literature to support the use of CT neck and chest without and with IV contrast in the initial staging of asymptomatic adult patients with ALL.

## CT Neck and Chest Without IV Contrast

There is no relevant literature to support the use of CT neck and chest without IV contrast in the initial staging of asymptomatic adult patients with ALL.

## **CTA Chest Abdomen Pelvis With IV Contrast**

There is no relevant literature to support the use of CTA chest, abdomen, and pelvis with IV contrast in the initial staging of asymptomatic adult patients with ALL.

## FDG-PET/CT Skull Base To Mid-Thigh

There are multiple case reports of FDG-PET/CT identifying extramedullary sites of disease in ALL; however, currently, there are no large, published studies supporting the use of FDG-PET/CT skull base to mid-thigh for the evaluation of ALL in an asymptomatic adult patient.

## FDG-PET/CT Whole Body

There are multiple case reports of FDG-PET/CT identifying extramedullary sites of disease in ALL; however, currently, there are no large, published studies supporting the use of FDG-PET/CT whole body for the evaluation of ALL in an asymptomatic adult patient.

## MRA Chest Abdomen Pelvis With IV Contrast

There is no relevant literature to support the use of MRA chest, abdomen, and pelvis with IV contrast in the initial staging of asymptomatic adult patients with ALL.

## MRI Abdomen and Pelvis With IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis with IV contrast in the initial staging of asymptomatic adult patients with ALL.

## MRI Abdomen and Pelvis Without and With IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis without and with IV contrast in the initial staging of asymptomatic adult patients with ALL.

## MRI Abdomen and Pelvis Without IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis without IV contrast in the initial staging of asymptomatic adult patients with ALL.

## MRI Abdomen Without and With IV Contrast

There is no relevant literature to support the use of MRI abdomen without and with IV contrast in the initial staging of asymptomatic adult patients with ALL.

## MRI Abdomen Without IV Contrast

There is no relevant literature to support the use of MRI abdomen without IV contrast in the initial staging of asymptomatic adult patients with ALL.

## MRI Chest Abdomen Pelvis Without and With IV Contrast

There is no relevant literature to support the use of MRI chest, abdomen, and pelvis without and with IV contrast in the initial staging of asymptomatic adult patients with ALL.

## MRI Chest Abdomen Pelvis Without IV Contrast

There is no relevant literature to support the use of MRI chest, abdomen, and pelvis without IV contrast in the initial staging of asymptomatic adult patients with ALL.

## MRI Head Without and With IV Contrast

There is no relevant literature to support the use of MRI head without and with IV contrast in the initial staging of asymptomatic adult patients with ALL.

## MRI Head Without IV Contrast

There is no relevant literature to support the use of MRI head without IV contrast in the initial staging of asymptomatic adult patients with ALL.

## Nuclear Medicine Ventriculography

There is no relevant literature to support the use of nuclear medicine ventriculography in the initial staging of asymptomatic adult patients with ALL.

# **Radiography Chest**

There is no relevant literature to support the use of chest radiography in the initial staging of asymptomatic adult patients with ALL.

## **Radiography Chest Abdomen Pelvis**

There is no relevant literature to support the use of radiography chest, abdomen, and pelvis in the initial staging of asymptomatic adult patients with ALL.

#### **Radiography Skeletal Survey**

There is no relevant literature to support the use of radiography skeletal survey in the initial staging of asymptomatic adult patients with ALL.

# Variant 4: Adult. Posttherapy evaluation of acute lymphoblastic leukemia with extra medullary disease at diagnosis.

Imaging of patients after treatment, who had prior extramedullary involvement by ALL, can ensure the disease is responding and provide necessary information while planning additional treatment options. The information provided by imaging helps identify patients who did not respond to the initial treatment and reduces potential delays to the starting the next line of therapy.

#### **Bone Scan Whole Body**

There is no relevant literature to support the use of whole body bone scan in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

## **CT Abdomen and Pelvis With IV Contrast**

There is no relevant literature to support the use of CT abdomen and pelvis with IV contrast in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

## CT Abdomen and Pelvis Without and With IV Contrast

There is no relevant literature to support the use of CT abdomen and pelvis without and with IV contrast in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

#### CT Abdomen and Pelvis Without IV Contrast

There is no relevant literature to support the use of CT abdomen and pelvis without IV contrast in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

## **CT Chest Abdomen Pelvis With IV Contrast**

In adult patients with extramedullary disease at diagnosis, a CT chest, abdomen, and pelvis with IV contrast is recommended by the NCCN guidelines to assess disease response [12].

## CT Chest Abdomen Pelvis Without and With IV Contrast

There is no relevant literature to support the use of CT chest, abdomen, and pelvis without and with IV contrast in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

## CT Chest Abdomen Pelvis Without IV Contrast

There is no relevant literature to support the use of CT chest, abdomen, and pelvis without IV contrast in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

#### **CT Chest With IV Contrast**

There is no relevant literature to support the use of CT chest with IV contrast in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

## CT Chest Without and With IV Contrast

There is no relevant literature to support the use of CT chest without and with IV contrast in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

#### **CT Chest Without IV Contrast**

There is no relevant literature to support the use of CT chest without IV contrast in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

## **CT Head With IV Contrast**

If the patients had extramedullary disease identified on prior CT head with IV contrast, then follow-up imaging should be obtained to evaluate for treatment response according to the NCCN guidelines [12].

## **CT Head Without and With IV Contrast**

There is no relevant literature to support the use of CT head without and with IV contrast in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

#### **CT Head Without IV Contrast**

There is no relevant literature to support the use of CT head without IV contrast in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

#### CT Neck and Chest With IV Contrast

In patients with extramedullary disease at diagnosis on prior CT neck and chest imaging, then a repeat CT neck and chest with IV contrast is recommended by the NCCN guidelines to assess disease response [12].

#### CT Neck and Chest Without and With IV Contrast

There is no relevant literature to support the use of CT neck and chest without and with IV contrast in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

#### **CT Neck and Chest Without IV Contrast**

There is no relevant literature to support the use of CT neck and chest without IV contrast in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

#### **CTA Chest Abdomen Pelvis With IV Contrast**

There is no relevant literature to support the use of CTA chest, abdomen, and pelvis with IV contrast in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

#### FDG-PET/CT Skull Base To Mid-Thigh

Current NCCN guidelines recommend FDG-PET/CT to assess treatment response, particularly if the patient had prior FDG-PET avid disease [12]. Additionally, a retrospective study of 180 patients with non-CNS extramedullary B-cell ALL treated with CAR T cells found that FDG-PET/CT imaging was necessary for monitoring and identifying areas of disease [13].

#### **FDG-PET/CT Whole Body**

Current NCCN guidelines recommend FDG-PET/CT to assess treatment response, particularly if the patient had prior FDG-PET avid disease [12]. Additionally, a retrospective study of 180 patients with non-CNS extramedullary B-cell ALL treated with CAR T cells found that FDG-PET/CT imaging was necessary for monitoring and identifying areas of disease [13].

#### MRA Chest Abdomen Pelvis With IV Contrast

There is no relevant literature to support the use of MRA chest, abdomen, and pelvis with IV contrast in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

## MRI Abdomen and Pelvis With IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis with IV contrast in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

## MRI Abdomen and Pelvis Without and With IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis without and with IV contrast in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

#### MRI Abdomen and Pelvis Without IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis without IV contrast in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

#### **MRI Abdomen Without and With IV Contrast**

There is no relevant literature to support the use of MRI abdomen without and with IV contrast in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

#### MRI Abdomen Without IV Contrast

There is no relevant literature to support the use of MRI abdomen without IV contrast in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

## MRI Chest Abdomen Pelvis Without and With IV Contrast

There is no relevant literature to support the use of MRI chest, abdomen, and pelvis without and with IV contrast in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

## MRI Chest Abdomen Pelvis Without IV Contrast

There is no relevant literature to support the use of MRI chest, abdomen, and pelvis without IV contrast in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

#### MRI Head Without and With IV Contrast

There is no relevant literature to support the use of MRI head without and with IV contrast in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

#### **MRI Head Without IV Contrast**

There is no relevant literature to support the use of MRI head without IV contrast in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

#### **Radiography Chest**

There is no relevant literature to support the use of chest radiography of the in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

#### **Radiography Chest Abdomen Pelvis**

There is no relevant literature to support the use of radiography chest, abdomen, and pelvis in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

#### **Radiography Skeletal Survey**

There is no relevant literature to support the use of radiography skeletal survey in the posttherapy evaluation of adult patients with ALL with extra medullary disease at diagnosis.

## Variant 5: Adult. Asymptomatic. Initial staging for acute myeloid or promyelocytic leukemia.

Imaging of patients with AML or acute promyelocytic leukemia (APL) can improve the detection of extramedullary disease involvement, while also increasing the detection of secondary complications associated with the disease, such as pulmonary infections. Accurately identifying areas of disease involvement allows for appropriate treatment, which can improve patient outcomes. Additionally, identifying areas of infection before chemotherapy allows for optimized treatment and a decreased rate of complications.

#### **Bone Scan Whole Body**

There is no relevant literature to support the use of whole body bone scan in the initial staging of asymptomatic adult patients with AML or APL.

## **CT Abdomen and Pelvis With IV Contrast**

There is no relevant literature to support the use of CT abdomen and pelvis with IV contrast in the initial staging of asymptomatic adult patients with AML or APL.

## CT Abdomen and Pelvis Without and With IV Contrast

There is no relevant literature to support the use of CT abdomen and pelvis without or with IV contrast in the initial staging of asymptomatic adult patients with AML or APL.

## **CT Abdomen and Pelvis Without IV Contrast**

There is no relevant literature to support the use of CT abdomen and pelvis without IV contrast in the initial staging of asymptomatic adult patients with AML or APL.

## **CT** Chest Abdomen Pelvis With IV Contrast

There is no relevant literature to support the use of CT chest, abdomen, and pelvis with IV contrast in the initial staging of asymptomatic adult patients with AML or APL.

## CT Chest Abdomen Pelvis Without and With IV Contrast

There is no relevant literature to support the use of CT chest, abdomen, and pelvis without and with IV contrast in the initial staging of asymptomatic adult patients with AML or APL.

## **CT Chest Abdomen Pelvis Without IV Contrast**

There is no relevant literature to support the use of CT chest, abdomen, and pelvis without IV contrast in the initial staging of asymptomatic adult patients with AML or APL.

## **CT Chest With IV Contrast**

In a prospective cohort study of 107 patients with newly diagnosed AML, 18.7% (20/107) of patients were diagnosed with proven or probable invasive pulmonary aspergillosis during hospitalization for induction chemotherapy [14]. An additional prospective study of 198 patients with hematologic malignancies (including ALL and AML) found presymptomatic CT chest examination identified abnormalities in 36% of patients [11]. The multivariate analysis found patients with an abnormal baseline chest CT had an adjusted hazard ratio of 1.52 (95% CI, 1.27-5.03) [11]. An additional retrospective study of 145 asymptomatic patients with AML had a baseline CT chest without IV contrast and found 47 patients (36%) to have possible pneumonia [15]. The authors report multiple limitations; however, that suggested the possibility of overdiagnosis of invasive fungal disease [15].

In the rare cases of hyperleukocytic AML, there is an association with pulmonary complications and high early mortality. A retrospective study of 73 patients admitted to the hospital with AML and white blood cell count >100  $\times$  10/L found 58% (42 patients) had abnormal findings on chest radiographs [16]. Of these 18 had chest CT scans that demonstrated abnormalities, including 2 patients with acute pulmonary embolism [16].

## CT Chest Without and With IV Contrast

There is no relevant literature to support the use of CT chest without and with IV contrast in the initial staging of asymptomatic adult patients with AML or APL.

## **CT Chest Without IV Contrast**

In a prospective cohort study of 107 patients with newly diagnosed AML, 18.7% (20/107) of patients were diagnosed with proven or probable invasive pulmonary aspergillosis during hospitalization for induction chemotherapy [14]. An additional prospective study of 198 patients with hematologic malignancies (including ALL and AML) found presymptomatic CT chest examination identified abnormalities in 36% of patients [11]. The multivariate analysis found patients with an abnormal baseline chest CT had an adjusted hazard ratio of 1.52 (95% CI, 1.27-5.03) [11]. An additional retrospective study of 145 asymptomatic patients with AML had a baseline CT chest without IV contrast and found 47 patients (36%) to have possible pneumonia [15]. The authors report multiple limitations; however, that suggested the possibility of overdiagnosis of invasive fungal disease [15].

In the rare cases of hyperleukocytic AML, there is an association with pulmonary complications and high early mortality. A retrospective study of 73 patients admitted to the hospital with AML and white blood cell count >100  $\times$  10/L found 58% (42 patients) had abnormal findings on chest radiographs [16]. Of these, 18 had chest CT scans that demonstrated abnormalities, including 2 patients with acute pulmonary embolism [16].

## **CT Head With IV Contrast**

There is no relevant literature to support the use of CT head with IV contrast in the initial staging of asymptomatic adult patients with AML or APL. Per NCCN and European Society For Medical Oncology guidelines, a CT head with IV contrast is useful in patients with suspected leukemic meningitis [17,18].

# **CT Head Without and With IV Contrast**

There is no relevant literature to support the use of CT head without and with IV contrast in the initial staging of asymptomatic adult patients with AML or APL.

## **CT Head Without IV Contrast**

Although not useful at diagnosis, patients with APL are at an increased risk for intracranial hemorrhage, and it is a main cause of death in the first 30 days after initiation of treatment [19]. A CT head without IV contrast should be recommended if there is clinical concern for intracranial hemorrhage [18].

# CT Neck and Chest With IV Contrast

There is no relevant literature to support the use of CT neck and chest with IV contrast in the initial staging of asymptomatic adult patients with AML or APL.

# CT Neck and Chest Without and With IV Contrast

There is no relevant literature to support the use of CT neck and chest without and with IV contrast in the initial staging of asymptomatic adult patients with AML or APL.

# CT Neck and Chest Without IV Contrast

There is no relevant literature to support the use of CT neck and chest without IV contrast in the initial staging of asymptomatic adult patients with AML or APL.

## CTA Chest Abdomen Pelvis With IV Contrast

There is no relevant literature to support the use of CTA chest, abdomen, and pelvis with IV contrast in the initial staging of asymptomatic adult patients with AML or APL.

# FDG-PET/CT Skull Base To Mid-Thigh

A small prospective study of 26 newly diagnosed patients with AML found FDG-PET/CT identified twice as many patients with extramedullary disease than those identified by clinical examination (65% versus 31%) [20]. PET/CT also found more total extramedullary lesions (55) compared with clinical examination (15) [20]. These findings were supported by an additional small study, which showed FDG-PET/CT was able to detect extramedullary disease in 90% of patients [21].

## FDG-PET/CT Whole Body

A small prospective study of 26 newly diagnosed patients with AML found FDG-PET/CT identified twice as many patients with extramedullary disease than those identified by clinical examination (65% versus 31%) [20]. PET/CT also found more total extramedullary lesions (55) compared with clinical examination (15) [20]. These findings were supported by an additional small study, which showed FDG-PET/CT was able to detect extramedullary disease in 90% of patients [21].

## MRA Chest Abdomen Pelvis With IV Contrast

There is no relevant literature to support the use of MRA chest, abdomen, and pelvis with IV contrast in the initial staging of asymptomatic adult patients with AML or APL.

## MRI Abdomen and Pelvis With IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis with IV contrast in the initial staging of asymptomatic adult patients with AML or APL.

## MRI Abdomen and Pelvis Without and With IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis without and with IV contrast in the initial staging of asymptomatic adult patients with AML or APL.

## MRI Abdomen and Pelvis Without IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis without IV contrast in the initial staging of asymptomatic adult patients with AML or APL.

## MRI Abdomen Without and With IV Contrast

There is no relevant literature to support the use of MRI abdomen without and with IV contrast in the initial staging of asymptomatic adult patients with AML or APL.

## **MRI Abdomen Without IV Contrast**

There is no relevant literature to support the use of MRI abdomen without IV contrast in the initial staging of asymptomatic adult patients with AML or APL.

# MRI Chest Abdomen Pelvis Without and With IV Contrast

There is no relevant literature to support the use of MRI chest, abdomen, and pelvis without and with IV contrast in the initial staging of asymptomatic adult patients with AML or APL.

## MRI Chest Abdomen Pelvis Without IV Contrast

There is no relevant literature to support the use of MRI chest, abdomen, and pelvis without IV contrast in the initial staging of asymptomatic adult patients with AML or APL.

## MRI Head Without and With IV Contrast

There is no relevant literature to support the use of MRI head without and with IV contrast in the initial staging of asymptomatic adult patients with AML or APL.

## MRI Head Without IV Contrast

There is no relevant literature to support the use of MRI head without IV contrast in the initial staging of asymptomatic adult patients with AML or APL.

## Nuclear Medicine Ventriculography

There is no relevant literature to support the use of nuclear medicine ventriculography in the initial staging of asymptomatic adult patients with AML or APL.

## **Radiography Chest**

In the rare cases of hyperleukocytic AML, there is an association with pulmonary complications and high early mortality. A retrospective study of 73 patients admitted to the hospital with AML and white blood cell count >100  $\times$  10/L found 58% (42 patients) had abnormal findings on chest radiographs [16]. Of these, 18 had chest CT scans that demonstrated abnormalities, including 2 patients with acute pulmonary embolism [16].

## **Radiography Chest Abdomen Pelvis**

There is no relevant literature to support the use of radiography chest, abdomen, and pelvis in the initial staging of asymptomatic adult patients with AML or APL.

## **Radiography Skeletal Survey**

There is no relevant literature to support the use of radiography skeletal survey in the initial staging of asymptomatic adult patients with AML or APL.

## Variant 6: Adult. Asymptomatic. Initial staging for chronic myeloid leukemia.

Imaging of patients with chronic myeloid leukemia (CML) is not often used because it does not typically change staging or treatment. Although there may be select cases in which imaging is beneficial, it is often not indicated.

## **Bone Scan Whole Body**

There is no relevant literature to support the use of whole body bone scan in the initial staging of asymptomatic adult patients for CML.

## **CT** Abdomen and Pelvis With IV Contrast

There is no relevant literature to support the use of CT abdomen and pelvis with IV contrast in the initial staging of asymptomatic adult patients for CML.

## CT Abdomen and Pelvis Without and With IV Contrast

There is no relevant literature to support the use of CT abdomen and pelvis without and with IV contrast in the initial staging of asymptomatic adult patients for CML.

## **CT** Abdomen and Pelvis Without IV Contrast

There is no relevant literature to support the use of CT abdomen and pelvis without IV contrast in the initial staging of asymptomatic adult patients for CML.

# **CT Chest Abdomen Pelvis With IV Contrast**

There is no relevant literature to support the use of CT chest, abdomen, and pelvis with IV contrast in the initial staging of asymptomatic adult patients for CML.

## CT Chest Abdomen Pelvis Without and With IV Contrast

There is no relevant literature to support the use of CT chest, abdomen, and pelvis without and with IV contrast in the initial staging of asymptomatic adult patients for CML.

# **CT Chest Abdomen Pelvis Without IV Contrast**

There is no relevant literature to support the use of CT chest, abdomen, and pelvis without IV contrast in the initial staging of asymptomatic adult patients for CML.

## **CT Chest With IV Contrast**

There is no relevant literature to support the use of CT chest with IV contrast in the initial staging of asymptomatic adult patients for CML.

## CT Chest Without and With IV Contrast

There is no relevant literature to support the use of CT chest without and with IV contrast in the initial staging of asymptomatic adult patients for CML.

## **CT Chest Without IV Contrast**

There is no relevant literature to support the use of CT chest without IV contrast in the initial staging of asymptomatic adult patients for CML.

# **CT Head With IV Contrast**

There is no relevant literature to support the use of CT head with IV contrast in the initial staging of asymptomatic adult patients for CML.

## **CT Head Without and With IV Contrast**

There is no relevant literature to support the use of CT head without and with IV contrast in the initial staging of asymptomatic adult patients for CML.

## **CT Head Without IV Contrast**

There is no relevant literature to support the use of CT head without IV contrast in the initial staging of asymptomatic adult patients for CML.

#### CT Neck and Chest With IV Contrast

There is no relevant literature to support the use of CT neck and chest with IV contrast in the initial staging of asymptomatic adult patients for CML.

## CT Neck and Chest Without and With IV Contrast

There is no relevant literature to support the use of CT neck and chest without and with IV contrast in the initial staging of asymptomatic adult patients for CML.

#### **CT Neck and Chest Without IV Contrast**

There is no relevant literature to support the use of CT neck and chest without IV contrast in the initial staging of asymptomatic adult patients for CML.

#### **CTA Chest Abdomen Pelvis With IV Contrast**

There is no relevant literature to support the use of CTA chest, abdomen, and pelvis with IV contrast in the initial staging of asymptomatic adult patients for CML.

#### FDG-PET/CT Skull Base To Mid-Thigh

There is no relevant literature to support the use of FDG-PET/CT skull base to mid-thigh in the initial staging of asymptomatic adult patients for CML.

#### **FDG-PET/CT Whole Body**

There is no relevant literature to support the use of FDG-PET/CT whole body in the initial staging of asymptomatic adult patients for CML.

#### MRA Chest Abdomen Pelvis With IV Contrast

There is no relevant literature to support the use of MRA chest, abdomen, and pelvis with IV contrast in the initial staging of asymptomatic adult patients for CML.

#### **MRI Abdomen and Pelvis With IV Contrast**

There is no relevant literature to support the use of MRI abdomen and pelvis with IV contrast in the initial staging of asymptomatic adult patients for CML.

## MRI Abdomen and Pelvis Without and With IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis without and with IV contrast in the initial staging of asymptomatic adult patients for CML.

## MRI Abdomen and Pelvis Without IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis without IV contrast in the initial staging of asymptomatic adult patients for CML.

## MRI Abdomen Without and With IV Contrast

There is no relevant literature to support the use of MRI abdomen without and with IV contrast in the initial staging of asymptomatic adult patients for CML.

## **MRI Abdomen Without IV Contrast**

There is no relevant literature to support the use of MRI abdomen without IV contrast in the initial staging of asymptomatic adult patients for CML.

#### MRI Chest Abdomen Pelvis Without and With IV Contrast

There is no relevant literature to support the use of MRI chest, abdomen, and pelvis without and with IV contrast in the initial staging of asymptomatic adult patients for CML.

## MRI Chest Abdomen Pelvis Without IV Contrast

There is no relevant literature to support the use of MRI chest, abdomen, and pelvis without IV contrast in the initial staging of asymptomatic adult patients for CML.

## MRI Head Without and With IV Contrast

There is no relevant literature to support the use of MRI head without and with IV contrast in the initial staging of asymptomatic adult patients for CML.

#### MRI Head Without IV Contrast

There is no relevant literature to support the use of MRI head without IV contrast in the initial staging of asymptomatic adult patients for CML.

#### **Radiography Chest**

There is no relevant literature to support the use of chest radiography in the initial staging of asymptomatic adult patients for CML.

#### **Radiography Chest Abdomen Pelvis**

There is no relevant literature to support the use of radiography chest, abdomen, and pelvis in the initial staging of asymptomatic adult patients for CML.

#### **Radiography Skeletal Survey**

There is no relevant literature to support the use of radiography skeletal survey in the initial staging of asymptomatic adult patients for CML.

## Variant 7: Adult. Asymptomatic. Initial staging for chronic lymphocytic leukemia.

Imaging of patients with CLL can improve accurate staging of the patient, which ensures appropriate treatment. Accurately identifying areas of disease involvement can impact the stage of disease. Ensuring accurate staging allows for appropriate treatment, which can improve patient outcomes.

#### **Bone Scan Whole Body**

There is no relevant literature to support the use of whole body bone scan in the initial staging of asymptomatic adult patients with CLL.

#### **CT Abdomen and Pelvis With IV Contrast**

There is no relevant literature to support the use of CT abdomen and pelvis with IV contrast in the initial staging of asymptomatic adult patients with CLL.

## CT Abdomen and Pelvis Without and With IV Contrast

There is no relevant literature to support the use of CT abdomen and pelvis without and with IV contrast in the initial staging of asymptomatic adult patients with CLL.

## **CT Abdomen and Pelvis Without IV Contrast**

There is no relevant literature to support the use of CT abdomen and pelvis without IV contrast in the initial staging of asymptomatic adult patients with CLL.

## **CT Chest Abdomen Pelvis With IV Contrast**

A prospective study of 240 patients with Binet stage A CLL underwent total body CT imaging, which resulted in upstaging in 42 patients (17.5%), by identification of lymphadenopathy not found on clinical examination [22]. In addition, CT imaging found discordance in clinically identified lymphadenopathy in 11 patients [22]. These findings were clinically relevant because the progression-free survival was shorter for the patients who were upstaged by the CT findings, 71.2% compared with 87.4% for those who were lower stage (P = .001).

## CT Chest Abdomen Pelvis Without and With IV Contrast

There is no relevant literature to support the use of CT chest, abdomen, and pelvis without and with IV contrast in the initial staging of asymptomatic adult patients with CLL.

## **CT Chest Abdomen Pelvis Without IV Contrast**

There is no relevant literature to support the use of CT chest, abdomen, and pelvis without IV contrast in the initial staging of asymptomatic adult patients with CLL.

#### **CT Chest With IV Contrast**

There is no relevant literature to support the use of CT chest with IV contrast in the initial staging of asymptomatic adult patients with CLL.

## CT Chest Without and With IV Contrast

There is no relevant literature to support the use of CT chest without and with IV contrast in the initial staging of asymptomatic adult patients with CLL.

## **CT Chest Without IV Contrast**

There is no relevant literature to support the use of CT chest without IV contrast in the initial staging of asymptomatic adult patients with CLL.

## **CT Head With IV Contrast**

There is no relevant literature to support the use of CT head with IV contrast in the initial staging of asymptomatic adult patients with CLL.

## **CT Head Without and With IV Contrast**

There is no relevant literature to support the use of CT head without and with IV contrast in the initial staging of asymptomatic adult patients with CLL.

## **CT Head Without IV Contrast**

There is no relevant literature to support the use of CT head without IV contrast in the initial staging of asymptomatic adult patients with CLL.

## CT Neck and Chest With IV Contrast

There is no relevant literature to support the use of CT neck and chest with IV contrast in the initial staging of asymptomatic adult patients with CLL.

## CT Neck and Chest Without and With IV Contrast

There is no relevant literature to support the use of CT neck and chest without and with IV contrast in the initial staging of asymptomatic adult patients with CLL.

## CT Neck and Chest Without IV Contrast

There is no relevant literature to support the use of CT neck and chest without IV contrast in the initial staging of asymptomatic adult patients with CLL.

## **CTA Chest Abdomen Pelvis With IV Contrast**

There is no relevant literature to support the use of CTA chest, abdomen, and pelvis with IV contrast in the initial staging of asymptomatic adult patients with CLL.

# FDG-PET/CT Skull Base To Mid-Thigh

A retrospective study of 90 patients with CLL found that those with a higher maximum standardized uptake value  $(SUV_{max}) \ge 5$  were more likely to be symptomatic (P = .031), had bulky nodes (P = .012), and increased lactate dehydrogenase (P = .026) [23]. In addition, higher rates of trisomy 12 and 11q deletion, as well as Ki-67 expression >30%, were also seen in patients with an SUV<sub>max</sub>  $\ge 5$  [23].

## FDG-PET/CT Whole Body

A retrospective study of 90 patients with CLL found that those with a higher SUV<sub>max</sub>  $\geq$ 5 were more likely to be symptomatic (*P* = .031), had bulky nodes (*P* = .012), and had increased lactate dehydrogenase (*P* = .026) [23]. In addition, higher rates of trisomy 12 and 11q deletion, as well as Ki-67 expression >30%, were also seen in patients with an SUV<sub>max</sub>  $\geq$ 5 [23].

## MRA Chest Abdomen Pelvis With IV Contrast

There is no relevant literature to support the use of MRA chest, abdomen, and pelvis with IV contrast in the initial staging of asymptomatic adult patients with CLL.

## **MRI Abdomen and Pelvis With IV Contrast**

There is no relevant literature to support the use of MRI abdomen and pelvis with IV contrast in the initial staging of asymptomatic adult patients with CLL.

## MRI Abdomen and Pelvis Without and With IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis without and with IV contrast in the initial staging of asymptomatic adult patients with CLL.

## MRI Abdomen and Pelvis Without IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis without IV contrast in the initial staging for CLL.

## MRI Abdomen Without and With IV Contrast

There is no relevant literature to support the use of MRI abdomen without and with IV contrast in the initial staging of asymptomatic adult patients with CLL.

#### **MRI Abdomen Without IV Contrast**

There is no relevant literature to support the use of MRI abdomen without IV contrast in the initial staging of asymptomatic adult patients with CLL.

#### MRI Chest Abdomen Pelvis Without and With IV Contrast

There is no relevant literature to support the use of MRI chest, abdomen, and pelvis without and with IV contrast in the initial staging of asymptomatic adult patients with CLL.

#### **MRI Chest Abdomen Pelvis Without IV Contrast**

There is no relevant literature to support the use of MRI chest, abdomen, and pelvis without IV contrast in the initial staging of asymptomatic adult patients with CLL.

#### MRI Head Without and With IV Contrast

A retrospective single center study of 1,115 (26.7%) of 4,174 patients with CLL who underwent MRI CNS imaging to evaluate neurological symptoms [24]. Of those, 50 patients had findings that were suspicious for CNS malignancy, with 34 patients undergoing CNS tissue biopsy. The biopsies showed small lymphocytic lymphoma/CLL confirmed in 9 patients, Richter transformation in 12 patients, progressive multifocal leukoencephalopathy in 2 patients, vasculitis in 3 patients, other cancers in 6 (3 primary and 3 metastatic) patients, and normal tissue in 2 patients [24].

#### **MRI Head Without IV Contrast**

There is no relevant literature to support the use of MRI head without IV contrast in the initial staging of asymptomatic adult patients with CLL.

## **Radiography Chest**

There is no relevant literature to support the use of chest radiography in the initial staging of asymptomatic adult patients with CLL.

#### **Radiography Chest Abdomen Pelvis**

There is no relevant literature to support the use of radiography chest, abdomen, and pelvis in the initial staging of asymptomatic adult patients with CLL.

#### **Radiography Skeletal Survey**

There is no relevant literature to support the use of radiography skeletal survey in the initial staging of asymptomatic adult patients with CLL.

## Variant 8: Adult. Surveillance of chronic lymphocytic leukemia with suspected histologic transformation.

Imaging of patients with suspected transformation can improve early detection of disease progression, which allows for timely treatment and better patient outcomes. Because Richter's transformation means the disease has become more aggressive, it is important for patients to be assessed with imaging, so they can be treated appropriately, which can improve patient outcomes.

#### **Bone Scan Whole Body**

There is no relevant literature to support the use of whole body bone scan in the surveillance of CLL with suspected histologic transformation (ie, Richter syndrome).

## CT Abdomen and Pelvis With IV Contrast

There is no relevant literature to support the use of CT abdomen and pelvis with IV contrast in the surveillance of CLL with suspected histologic transformation (ie, Richter syndrome).

## CT Abdomen and Pelvis Without and With IV Contrast

There is no relevant literature to support the use of CT abdomen and pelvis without and with IV contrast in the surveillance of CLL with suspected histologic transformation (ie, Richter syndrome).

## CT Abdomen and Pelvis Without IV Contrast

There is no relevant literature to support the use of CT abdomen and pelvis without IV contrast in the surveillance of CLL with suspected histologic transformation (ie, Richter syndrome).

# **CT** Chest Abdomen Pelvis With IV Contrast

A retrospective study of 52 patients with either indolent CLL, aggressive CLL, or diffuse large B cell lymphoma from Richter transformation demonstrated that CT texture analysis features of ultrastructure and vascularization differ between CLL and diffuse large B cell lymphoma populations [25]. An additional retrospective study of 34 patients with suspected Richter transformation found contrast-enhanced CTs indicative of transformation in 20 patients [26]. This study found a histological and radiological concordance of 94% (positive predictive value [PPV] of 100%, negative predictive value [NPV] of 90%) [26].

# CT Chest Abdomen Pelvis Without and With IV Contrast

There is no relevant literature to support the use of CT chest, abdomen, and pelvis without and with IV contrast in the surveillance of CLL with suspected histologic transformation (ie, Richter syndrome).

## **CT Chest Abdomen Pelvis Without IV Contrast**

A retrospective study of 34 patients with suspected Richter transformation found contrast-enhanced CTs indicative of transformation in 20 patients [26]. This study found a histological and radiological concordance of 94% (PPV of 100%, NPV of 90%) [26].

# **CT Chest With IV Contrast**

There is no relevant literature to support the use of CT chest with IV contrast in the surveillance of CLL with suspected histologic transformation (ie, Richter syndrome).

## CT Chest Without and With IV Contrast

There is no relevant literature to support the use of CT chest without and with IV contrast in the surveillance of CLL with suspected histologic transformation (ie, Richter syndrome).

## **CT Chest Without IV Contrast**

There is no relevant literature to support the use of CT chest without IV contrast in the surveillance of CLL with suspected histologic transformation (ie, Richter syndrome).

## CT Neck and Chest With IV Contrast

There is no relevant literature to support the use of CT neck and chest with IV contrast in the surveillance of CLL with suspected histologic transformation (ie, Richter syndrome).

# CT Neck and Chest Without and With IV Contrast

There is no relevant literature to support the use of CT neck and chest without and with IV contrast in the surveillance of CLL with suspected histologic transformation (ie, Richter syndrome).

## CT Neck and Chest Without IV Contrast

There is no relevant literature to support the use of CT neck and chest without IV contrast in the surveillance of CLL with suspected histologic transformation (ie, Richter syndrome).

# **CTA Chest Abdomen Pelvis With IV Contrast**

There is no relevant literature to support the use of CTA chest, abdomen, and pelvis with IV contrast in the surveillance of CLL with suspected histologic transformation (ie, Richter syndrome).

# FDG-PET/CT Skull Base To Mid-Thigh

A retrospective study of 332 patients with CLL found Richter transformation was associated with a higher SUV<sub>max</sub> [27]. In addition, this study reported an SUV<sub>max</sub>  $\geq 10$  was strongly correlated with overall survival, with patients whose CLL had an SUV<sub>max</sub> of <10 demonstrating an overall survival of 56.7 months, compared with those whose SUV<sub>max</sub> was  $\geq 10$  and had an overall survival of 6.9 months [27]. FDG-PET/CT was also useful in identifying possible biopsy sites, which are most likely to have undergone transformation [27]. It should be noted that the sensitivity for the detection of transformation may decrease if the patients' CLL have previously been treated with venetoclax [28].

An additional retrospective study of 90 patients with suspected Richter transformation had an SUV<sub>max</sub> cutoff of  $\geq$ 5, sensitivity of 88.2%, specificity of 71.2%, PPV of 51.3%, and NPV of 94% [23]. This study also reported SUV values may be helpful in the prognostic stratification of CLL [23]. This is supported by a smaller prospective study

of patients with CLL, which found significant difference in  $SUV_{max}$  with the patients with CLL having a median of 3.1 and those with suspected or confirmed Richter transformation having a median  $SUV_{max}$  of 16.5 [29].

A retrospective study of 272 patients, who underwent a total of 526 FDG-PET/CT scans, 472 (89.7%) were found to be abnormal [30]. Of the 526 total PET/CT scans, 293 were used for routine evaluation of CLL, with the PET component being of clinical value in only 1 instance [30]. In 83 patients, the PET/CT was used to evaluate new clinical complications and to localize areas of high FDG avidity for biopsy. These resulted in relevant new diagnoses in 32 patients [30]. This study supports the role of FDG-PET/CT in the detection of aggressive transformations but also demonstrates that there is little value in PET/CT imaging for the routine surveillance of patients with CLL.

## FDG-PET/CT Whole Body

A retrospective study of 332 patients with CLL found Richter transformation was associated with a higher SUV<sub>max</sub> [27]. In addition, this study reported an SUV<sub>max</sub>  $\geq 10$  was strongly correlated with overall survival, with patients whose CLL had an SUV<sub>max</sub> of <10 demonstrating an overall survival of 56.7 months, compared with those whose SUV<sub>max</sub> was  $\geq 10$  and had an overall survival of 6.9 months [27]. FDG-PET/CT was also useful in identifying possible biopsy sites, which are most likely to have undergone transformation [27]. It should be noted that the sensitivity for detection of transformation may decrease if the patients' CLL have previously been treated with venetoclax [28].

An additional retrospective study of 90 patients with suspected Richter transformation had an SUV<sub>max</sub> cutoff of  $\geq$ 5, sensitivity of 88.2%, specificity of 71.2%, PPV of 51.3%, and NPV of 94% [23]. This study also reported that SUV values may be helpful in the prognostic stratification of CLL [23]. This is supported by a smaller prospective study of patients with CLL, which found significant difference in SUV<sub>max</sub>, with the patients with CLL having a median of 3.1 and those with suspected or confirmed Richter transformation having a median SUV<sub>max</sub> of 16.5 [29].

A retrospective study of 272 patients, who underwent a total of 526 FDG-PET/CT scans, 472 (89.7%) were found to be abnormal [30]. Of the 526 total PET/CT scans, 293 were used for routine evaluation of CLL, with the PET component being of clinical value in only 1 instance [30]. In 83 patients the PET/CT was used to evaluate new clinical complications and to localize areas of high FDG avidity for biopsy. These resulted in relevant new diagnoses in 32 patients [30]. This study supports the role of FDG-PET/CT in the detection of aggressive transformations but also demonstrates there is little value in PET/CT imaging for the routine surveillance of patients with CLL.

## **Gallium Scan Whole Body**

There is no relevant literature to support the use of gallium scan whole body imaging in the surveillance of CLL with suspected histologic transformation (ie, Richter syndrome).

# MRA Chest Abdomen Pelvis With IV Contrast

There is no relevant literature to support the use of MRA chest, abdomen, and pelvis with IV contrast in the surveillance of CLL with suspected histologic transformation (ie, Richter syndrome).

## MRI Abdomen and Pelvis With IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis with IV contrast in the surveillance of CLL with suspected histologic transformation (ie, Richter syndrome).

# MRI Abdomen and Pelvis Without and With IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis without and with IV contrast in the surveillance of CLL with suspected histologic transformation (ie, Richter syndrome).

# MRI Abdomen and Pelvis Without IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis without IV contrast in the surveillance of CLL with suspected histologic transformation (ie, Richter syndrome).

## MRI Abdomen Without and With IV Contrast

There is no relevant literature to support the use of MRI abdomen without and with IV contrast in the surveillance of CLL with suspected histologic transformation (ie, Richter syndrome).

# **MRI Abdomen Without IV Contrast**

There is no relevant literature to support the use of MRI abdomen without IV contrast in the surveillance of CLL with suspected histologic transformation (ie, Richter syndrome).

## MRI Chest Abdomen Pelvis Without and With IV Contrast

There is no relevant literature to support the use of MRI chest, abdomen, and pelvis without and with IV contrast in the surveillance of CLL with suspected histologic transformation (ie, Richter syndrome).

## MRI Chest Abdomen Pelvis Without IV Contrast

There is no relevant literature to support the use of MRI chest, abdomen, and pelvis without IV contrast in the surveillance of CLL with suspected histologic transformation (ie, Richter syndrome).

#### **Radiography Chest**

There is no relevant literature to support the use of chest radiography in the surveillance of CLL with suspected histologic transformation (ie, Richter syndrome).

#### **Radiography Chest Abdomen Pelvis**

There is no relevant literature to support the use of radiography chest, abdomen, and pelvis in the surveillance of CLL with suspected histologic transformation (ie, Richter syndrome).

## Variant 9: Adult. Asymptomatic. Initial staging for hairy cell leukemia.

Imaging of patients with hairy cell leukemia can improve the detection of lymphadenopathy, which can be monitored for treatment response. Accurately identifying areas of disease involvement allows for improved patient monitoring, which can improve patient outcomes.

#### **Bone Scan Whole Body**

There is no relevant literature to support the use of whole body bone scan in the initial staging of asymptomatic adult patients with hairy cell leukemia.

## CT Abdomen and Pelvis With IV Contrast

There is no relevant literature to support the use of CT abdomen and pelvis with IV contrast in the initial staging of asymptomatic adult patients with hairy cell leukemia.

#### CT Abdomen and Pelvis Without and With IV Contrast

There is no relevant literature to support the use of CT abdomen and pelvis without and with IV contrast in the initial staging for hairy cell leukemia.

#### CT Abdomen and Pelvis Without IV Contrast

There is no relevant literature to support the use of CT abdomen and pelvis without IV contrast in the initial staging of asymptomatic adult patients with hairy cell leukemia.

## **CT Chest Abdomen Pelvis With IV Contrast**

The British Committee for Standards in Haematology report CT chest, abdomen, and pelvis with IV contrast imaging may be beneficial to evaluate for sites of lymphadenopathy, which can be monitored for response [31].

## CT Chest Abdomen Pelvis Without and With IV Contrast

There is no relevant literature to support the use of CT chest, abdomen, and pelvis without and with IV contrast in the initial staging of asymptomatic adult patients with hairy cell leukemia.

#### **CT Chest Abdomen Pelvis Without IV Contrast**

The British Committee for Standards in Haematology report CT chest, abdomen, and pelvis without IV contrast imaging may be beneficial to evaluate for sites of lymphadenopathy, which can be monitored for response [31].

## **CT Chest With IV Contrast**

There is no relevant literature to support the use of CT chest with IV contrast in the initial staging of asymptomatic adult patients with hairy cell leukemia.

## CT Chest Without and With IV Contrast

There is no relevant literature to support the use of CT chest without and with IV contrast in the initial staging of asymptomatic adult patients with hairy cell leukemia.

#### **CT Chest Without IV Contrast**

There is no relevant literature to support the use of CT chest without IV contrast in the initial staging of asymptomatic adult patients with hairy cell leukemia.

## **CT Head With IV Contrast**

There is no relevant literature to support the use of CT head with IV contrast in the initial staging of asymptomatic adult patients with hairy cell leukemia.

## **CT Head Without and With IV Contrast**

There is no relevant literature to support the use of CT head without and with IV contrast in the initial staging of asymptomatic adult patients with hairy cell leukemia.

#### **CT Head Without IV Contrast**

There is no relevant literature to support the use of CT head without IV contrast in the initial staging of asymptomatic adult patients with hairy cell leukemia.

#### CT Neck and Chest With IV Contrast

There is no relevant literature to support the use of CT neck and chest with IV contrast in the initial staging of asymptomatic adult patients with hairy cell leukemia.

#### CT Neck and Chest Without and With IV Contrast

There is no relevant literature to support the use of CT neck and chest without and with IV contrast in the initial staging of asymptomatic adult patients with hairy cell leukemia.

#### **CT Neck and Chest Without IV Contrast**

There is no relevant literature to support the use of CT neck and chest without IV contrast in the initial staging of asymptomatic adult patients with hairy cell leukemia.

#### **CTA Chest Abdomen Pelvis With IV Contrast**

There is no relevant literature to support the use of CTA chest, abdomen, and pelvis with IV contrast in the initial staging of asymptomatic adult patients with hairy cell leukemia.

#### FDG-PET/CT Skull Base To Mid-Thigh

There are case reports of FDG-PET/CT identifying sites of otherwise occult disease; however, there are no larger studies to support the use of FDG-PET/CT in initial staging of hairy cell leukemia [32,33].

#### FDG-PET/CT Whole Body

There are case reports of FDG-PET/CT identifying sites of otherwise occult disease; however, there are no larger studies to support the use of FDG-PET/CT in initial staging of hairy cell leukemia [32,33].

#### MRA Chest Abdomen Pelvis With IV Contrast

There is no relevant literature to support the use of MRA chest, abdomen, and pelvis with IV contrast in the initial staging of asymptomatic adult patients with hairy cell leukemia.

## MRI Abdomen and Pelvis With IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis with IV contrast in the initial staging of asymptomatic adult patients with hairy cell leukemia.

#### MRI Abdomen and Pelvis Without and With IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis without and with IV contrast in the initial staging for hairy cell leukemia.

#### MRI Abdomen and Pelvis Without IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis without IV contrast in the initial staging for hairy cell leukemia.

#### MRI Abdomen Without and With IV Contrast

There is no relevant literature to support the use of MRI abdomen without and with IV contrast in the initial staging of asymptomatic adult patients with hairy cell leukemia.

#### MRI Abdomen Without IV Contrast

There is no relevant literature to support the use of MRI abdomen without IV contrast in the initial staging for hairy cell leukemia.

## MRI Chest Abdomen Pelvis Without and With IV Contrast

There is no relevant literature to support the use of MRI chest, abdomen, and pelvis without and with IV contrast in the initial staging of asymptomatic adult patients with hairy cell leukemia.

## **MRI Chest Abdomen Pelvis Without IV Contrast**

There is no relevant literature to support the use of MRI chest, abdomen, and pelvis without IV contrast in the initial staging of asymptomatic adult patients with hairy cell leukemia.

## MRI Head Without and With IV Contrast

There is no relevant literature to support the use of MRI head without and with IV contrast in the initial staging of asymptomatic adult patients with hairy cell leukemia.

#### **MRI Head Without IV Contrast**

There is no relevant literature to support the use of MRI head without IV contrast in the initial staging of asymptomatic adult patients with hairy cell leukemia.

#### **Radiography Chest**

There is no relevant literature to support the use of chest radiography in the initial staging of asymptomatic adult patients with hairy cell leukemia.

#### **Radiography Chest Abdomen Pelvis**

There is no relevant literature to support the use of radiography chest, abdomen, and pelvis in the initial staging of asymptomatic adult patients with hairy cell leukemia.

#### **Radiography Skeletal Survey**

There is no relevant literature to support the use of radiography skeletal survey in the initial staging of asymptomatic adult patients with hairy cell leukemia.

#### **US Abdomen**

There is no relevant literature to support the use of US in the initial staging of asymptomatic adult patients with hairy cell leukemia.

#### Summary of Highlights

This is a summary of the key recommendations from the variant tables. Refer to the complete narrative document for more information.

- Variant 1: For the initial staging of a male child with newly diagnosed ALL, no imaging is categorized as usually appropriate. Both US of the scrotum and chest radiography may be appropriate, although there is disagreement among the panel members. US of the scrotum can be used to exclude testicular involvement by ALL, which is supported by NCCN; however, it is not often used in clinical practice. Prior research has demonstrated that a chest radiograph may detect intrathoracic lesions, although it is not used for staging.
- Variant 2: For the initial staging of a female child with newly diagnosed ALL, no imaging is categorized as usually appropriate. Chest radiography may be appropriate, although there is disagreement among the panel regarding the use of chest radiography. Prior research has demonstrated that a chest radiograph may detect intrathoracic lesions, although it is not used for staging.
- Variant 3: For the initial staging of an adult asymptomatic patient with newly diagnosed ALL, no imaging is categorized as usually appropriate. CT chest without IV contrast may be appropriate for detection of intrathoracic abnormalities because prior research has demonstrated an elevated hazard ratio with intrathoracic abnormalities; however, there is disagreement among the panel members of the usefulness of such imaging in asymptomatic patients.
- Variant 4: For the posttherapy evaluation of adults with ALL and extra medullary disease at diagnosis, CT chest, abdomen, and pelvis with IV contrast, FDG-PET/CT skull base to mid-thigh, or FDG-PET/CT whole body are usually appropriate to assess disease response. The information provided by imaging helps identify patients who did not respond to the initial treatment and reduces potential delays to the starting of the next line of therapy.
- Variant 5: For adults who are asymptomatic needing initial staging for acute myeloid or promyelocytic leukemia FDG-PET/CT skull base to mid-thigh or FDG-PET/CT whole body imaging is usually appropriate. FDG-PET/CT has demonstrated improved the detection of extramedullary disease involvement, while also increasing the detection of secondary complications associated with the disease, such as pulmonary infections. Accurately identifying areas of disease involvement allows for appropriate treatment, which can improve patient outcomes.

- Variant 6: For asymptomatic adults undergoing initial staging for CML, no imaging is usually appropriate. Initial workup for adults with CML includes physical examination, laboratory testing, and bone marrow biopsy.
- Variant 7: For asymptomatic adults undergoing initial staging for CLL, no imaging is usually appropriate. There is disagreement among the panel on whether CT chest, abdomen, and pelvis with IV contrast, FDG-PET/CT skull base to mid-thigh or FDG-PET/CT whole body may be appropriate in asymptomatic adults. CT chest, abdomen, and pelvis with IV contrast has been reported to result in upstaging of a small portion of patients, as well as defining discordance in clinically identified lymphadenopathy. Both of which were clinically relevant because the progression-free survival was shorter for the patients who were upstaged by the CT findings. Similarly, FDG-PET/CT skull base to mid-thigh and FDG-PET/CT whole body imaging found that lesions with increased SUV were more likely to have higher rates of trisomy 12 and 11q deletion, as well as Ki-67 expression >30%.
- Variant 8: For adults with CLL and suspected histologic transformation (ie, Richter syndrome). CT chest, abdomen, and pelvis with IV contrast, FDG-PET/CT skull base to mid-thigh or FDG-PET/CT whole body is usually appropriate. CT chest, abdomen, and pelvis with IV contrast has been reported to have a high concordance rate to histological evaluation (94%). FDG-PET/CT based imaging is useful in both the detection of FDG avid lymph nodes and to assist in selection of targeted biopsy sites on the background of diffuse lymphadenopathy associated with CLL.
- Variant 9: For asymptomatic adults undergoing initial staging for hairy cell leukemia. No imaging is usually appropriate, however, CT chest, abdomen, and pelvis with or without IV contrast may be appropriate to identify sites of lymphadenopathy, which can be used to assess treatment response.

## **Supporting Documents**

The evidence table, literature search, and appendix for this topic are available at <u>https://acsearch.acr.org/list</u>. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents, click <u>here</u>.

## Gender Equality and Inclusivity Clause

The ACR acknowledges the limitations in applying inclusive language when citing research studies that pre-dates the use of the current understanding of language inclusive of diversity in sex, intersex, gender and gender-diverse people. The data variables regarding sex and gender used in the cited literature will not be changed. However, this guideline will use the terminology and definitions as proposed by the National Institutes of Health [34].

#### **Appropriateness Category Names and Definitions**

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

## **Relative Radiation Level Information**

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria<sup>®</sup> Radiation Dose Assessment Introduction document [35].

Relative Radiation Level Designations		
Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
0	0 mSv	0 mSv
۲	<0.1 mSv	<0.03 mSv
	0.1-1 mSv	0.03-0.3 mSv
	1-10 mSv	0.3-3 mSv
	10-30 mSv	3-10 mSv
	30-100 mSv	10-30 mSv

\*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."

## **References**

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. CA Cancer J Clin 2022;72:7-33.

- 2. American College of Radiology. ACR-NASCI-SIR-SPR Practice Parameter for the Performance and Interpretation of Body Computed Tomography Angiography (CTA). Available at: <u>https://gravitas.acr.org/PPTS/GetDocumentView?docId=164+&releaseId=2</u>. Accessed March 31, 2025.
- 3. Fujiki T, Nishimura R, Mase S, et al. Accurate detection of renal leukemic involvement in children using 3-D computed tomography modeling. Pediatr Int 2019;61:679-87.
- 4. Brown P, Inaba H, Annesley C, et al. Pediatric Acute Lymphoblastic Leukemia, Version 2.2020, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw 2020;18:81-112.
- 5. Krull K, Kunstreich M, Bronsema A, et al. Osteonecrosis in children with acute lymphoblastic leukemia at initial diagnosis and prior to any chemotherapy. Leuk Lymphoma 2019;60:78-84.
- Cao W, Liang C, Gen Y, Wang C, Zhao C, Sun L. Role of diffusion-weighted imaging for detecting bone marrow infiltration in skull in children with acute lymphoblastic leukemia. Diagn Interv Radiol 2016;22:580-86.
- 7. Pryweller JR, Glass JO, Sabin ND, et al. Characterization of Leukoencephalopathy and Association With Later Neurocognitive Performance in Pediatric Acute Lymphoblastic Leukemia. Invest Radiol 2021;56:117-26.
- 8. Lauer M, Kernen E, Schwabe D, Lehrnbecher T, Porto L. The role of magnetic resonance imaging in the diagnosis of central nervous system involvement in children with acute lymphoblastic leukemia. Pediatr Blood Cancer 2020;67:e28294.
- 9. Ranta S, Palomaki M, Levinsen M, et al. Role of neuroimaging in children with acute lymphoblastic leukemia and central nervous system involvement at diagnosis. Pediatr Blood Cancer 2017;64:64-70.
- 10. Smith WT, Shiao KT, Varotto E, et al. Evaluation of Chest Radiographs of Children with Newly Diagnosed Acute Lymphoblastic Leukemia. J Pediatr 2020;223:120-27 e3.
- 11. Ceesay MM, Desai SR, Cleverley J, et al. Pre-symptomatic (Baseline) computed tomography predicts invasive pulmonary aspergillosis in high-risk adult haemato-oncology patients. Br J Haematol 2018;182:723-27.
- 12. Brown PA, Shah B, Advani A, et al. Acute Lymphoblastic Leukemia, Version 2.2021, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw 2021;19:1079-109.
- 13. Holland EM, Yates B, Ling A, et al. Characterization of extramedullary disease in B-ALL and response to CAR T-cell therapy. Blood Adv 2022;6:2167-82.
- 14. Bitterman R, Hardak E, Raines M, et al. Baseline Chest Computed Tomography for Early Diagnosis of Invasive Pulmonary Aspergillosis in Hemato-oncological Patients: A Prospective Cohort Study. Clin Infect Dis 2019;69:1805-08.
- 15. Vallipuram J, Dhalla S, Bell CM, et al. Chest CT scans are frequently abnormal in asymptomatic patients with newly diagnosed acute myeloid leukemia. Leuk Lymphoma 2017;58:834-41.
- Stefanski M, Jamis-Dow C, Bayerl M, Desai RJ, Claxton DF, Van de Louw A. Chest radiographic and CT findings in hyperleukocytic acute myeloid leukemia: A retrospective cohort study of 73 patients. Medicine (Baltimore) 2016;95:e5285.
- 17. Heuser M, Ofran Y, Boissel N, et al. Acute myeloid leukaemia in adult patients: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2020;31:697-712.
- 18. Pollyea DA, Bixby D, Perl A, et al. NCCN Guidelines Insights: Acute Myeloid Leukemia, Version 2.2021. J Natl Compr Canc Netw 2021;19:16-27.
- 19. Gurnari C, Breccia M, Di Giuliano F, et al. Early intracranial haemorrhages in acute promyelocytic leukaemia: analysis of neuroradiological and clinico-biological parameters. Br J Haematol 2021;193:129-32.
- 20. Cribe AS, Steenhof M, Marcher CW, Petersen H, Frederiksen H, Friis LS. Extramedullary disease in patients with acute myeloid leukemia assessed by 18F-FDG PET. Eur J Haematol 2013;90:273-8.
- 21. Stolzel F, Rollig C, Radke J, et al. (1)(8)F-FDG-PET/CT for detection of extramedullary acute myeloid leukemia. Haematologica 2011;96:1552-6.
- 22. Gentile M, Cutrona G, Fabris S, et al. Total body computed tomography scan in the initial work-up of Binet stage A chronic lymphocytic leukemia patients: Results of the prospective, multicenter O-CLL1-GISL study. Am J Hematol 2013;88:539-44.
- 23. Mauro FR, Chauvie S, Paoloni F, et al. Diagnostic and prognostic role of PET/CT in patients with chronic lymphocytic leukemia and progressive disease. Leukemia 2015;29:1360-5.
- 24. Strati P, Uhm JH, Kaufmann TJ, et al. Prevalence and characteristics of central nervous system involvement by chronic lymphocytic leukemia. Haematologica 2016;101:458-65.
- 25. Reinert CP, Federmann B, Hofmann J, et al. Computed tomography textural analysis for the differentiation of chronic lymphocytic leukemia and diffuse large B cell lymphoma of Richter syndrome. Eur Radiol 2019;29:6911-21.

- 26. Federmann B, Mueller MR, Steinhilber J, Horger MS, Fend F. Diagnosis of Richter transformation in chronic lymphocytic leukemia: histology tips the scales. Ann Hematol 2018;97:1859-68.
- 27. Falchi L, Keating MJ, Marom EM, et al. Correlation between FDG/PET, histology, characteristics, and survival in 332 patients with chronic lymphoid leukemia. Blood 2014;123:2783-90.
- 28. Mato AR, Wierda WG, Davids MS, et al. Utility of positron emission tomography-computed tomography in patients with chronic lymphocytic leukemia following B-cell receptor pathway inhibitor therapy. Haematologica 2019;104:2258-64.
- 29. Papajik T, Myslivecek M, Urbanova R, et al. 2-[18F]fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography examination in patients with chronic lymphocytic leukemia may reveal Richter transformation. Leuk Lymphoma 2014;55:314-9.
- 30. Conte MJ, Bowen DA, Wiseman GA, et al. Use of positron emission tomography-computed tomography in the management of patients with chronic lymphocytic leukemia/small lymphocytic lymphoma. Leuk Lymphoma 2014;55:2079-84.
- 31. Jones G, Parry-Jones N, Wilkins B, Else M, Catovsky D, British Committee for Standards in H. Revised guidelines for the diagnosis and management of hairy cell leukaemia and hairy cell leukaemia variant\*. Br J Haematol 2012;156:186-95.
- 32. Robak P, Jesionek-Kupnicka D, Kupnicki P, Polliack A, Robak T. Multifocal osteolytic lesions in hairy cell leukemia-the importance of PET/CT in diagnosis and assessment. Ann Hematol 2021;100:1641-45.
- 33. Gibson G, Lai J, Thomas P. Unusual soft tissue infiltrates with 18F-FDG uptake in a patient with hairy cell leukemia. Clin Nucl Med 2015;40:e282-4.
- 34. National Academies of Sciences, Engineering, and Medicine; Division of Behavioral and Social Sciences and Education; Committee on National Statistics; Committee on Measuring Sex, Gender Identity, and Sexual Orientation. Measuring Sex, Gender Identity, and Sexual Orientation. In: Becker T, Chin M, Bates N, eds. Measuring Sex, Gender Identity, and Sexual Orientation. Washington (DC): National Academies Press (US) Copyright 2022 by the National Academy of Sciences. All rights reserved.; 2022.
- 35. American College of Radiology. ACR Appropriateness Criteria<sup>®</sup> Radiation Dose Assessment Introduction. Available at: <u>https://edge.sitecorecloud.io/americancoldf5f-acrorgf92a-productioncb02-3650/media/ACR/Files/Clinical/Appropriateness-Criteria/ACR-Appropriateness-Criteria-Radiation-Dose-Assessment-Introduction.pdf</u>. Accessed March 31, 2025.

The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.