Prognosis of chronic lymphocytic leukaemia (CLL)

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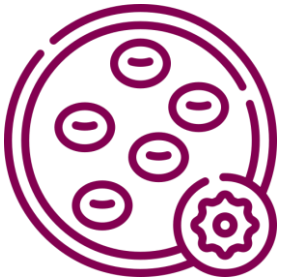
Clinical staging

- The 2 widely-used staging systems in CLL are the **Rai system** and the **Binet system**[1]
- Both systems stratify people into **prognostic groups** based on:[1]

Physical examination

- Lymphadenopathy
- Hepatomegaly
- Splenomegaly

Blood count



- Anaemia
- Thrombocytopenia

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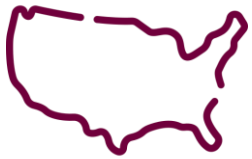
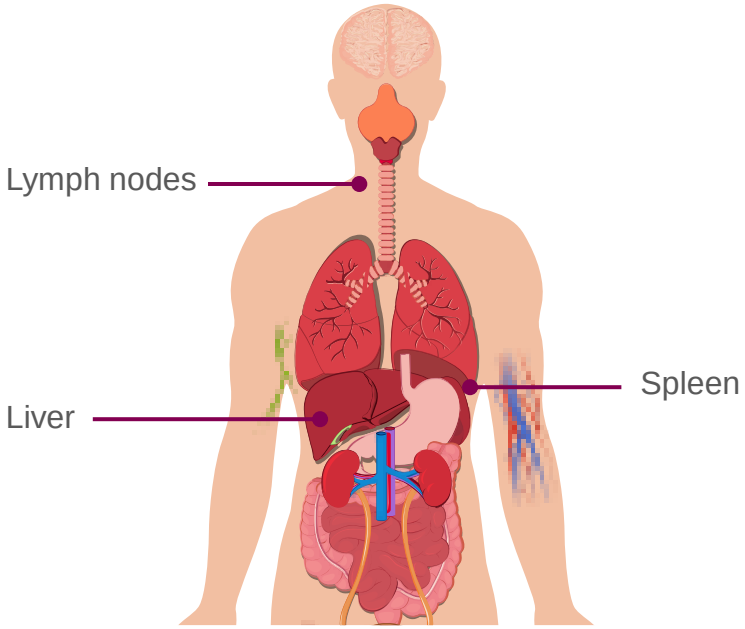
Rai versus Binet staging systems: overview

Rai system



Mainly used in:
United States*[1]

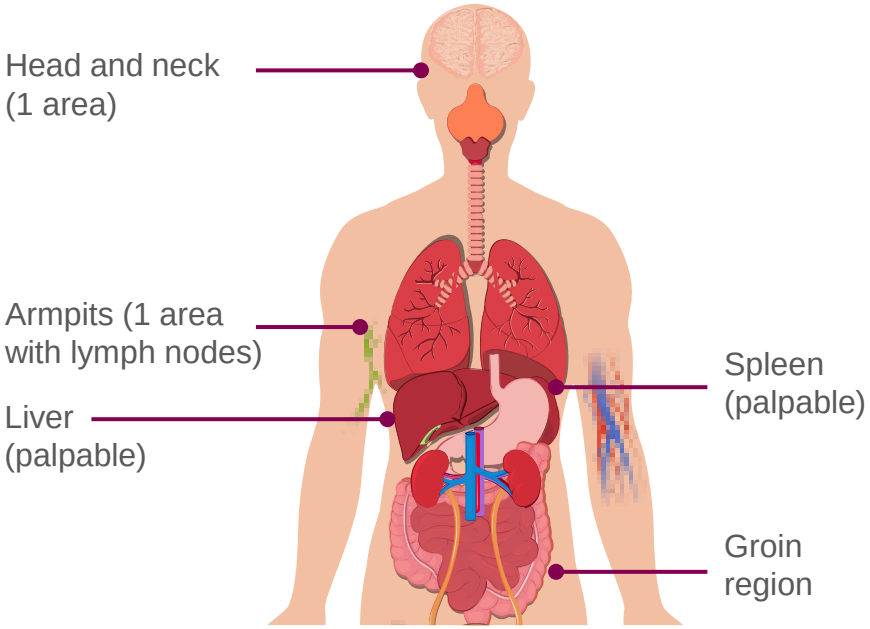
Based on: organ involvement[2]



Binet system

Mainly used in:
Europe*[1]

Based on: number of areas involved, as defined by the presence of enlarged lymph nodes (>1 cm in diameter or organomegaly)[2]



*Both staging systems are used in Asia

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Rai versus Binet staging systems: stages

Rai system

Stage	Description[3,4]
Stage 0 (Low risk)	• Lymphocytosis only
Stage I (Intermediate risk)	• Lymphocytosis and lymphadenopathy
Stage II (Intermediate risk)	• Lymphocytosis with splenomegaly or hepatomegaly • Lymphadenopathy irrelevant
Stage III (High risk)	• Lymphocytosis with anaemia (Hb <11 g/dL) • Organomegaly and lymphadenopathy irrelevant
Stage IV (High risk)	• Lymphocytosis with thrombocytopenia (platelets <100,000/μL) • Organomegaly, lymphadenopathy and anaemia irrelevant

Binet system

Stage	Description[3,4]
Stage A	• <3 nodal areas involved (including liver and spleen) • Haemoglobin ≥10 g/dL • Platelets ≥100,000/μL
Stage B	• ≥3 nodal areas involved (including liver and spleen) • Haemoglobin ≥10 g/dL • Platelets ≥100,000/μL
Stage C	• Anaemia (Hb <10 g/dL) and/or thrombocytopenia (platelets <100,000/μL) • Organomegaly and nodal enlargement irrelevant

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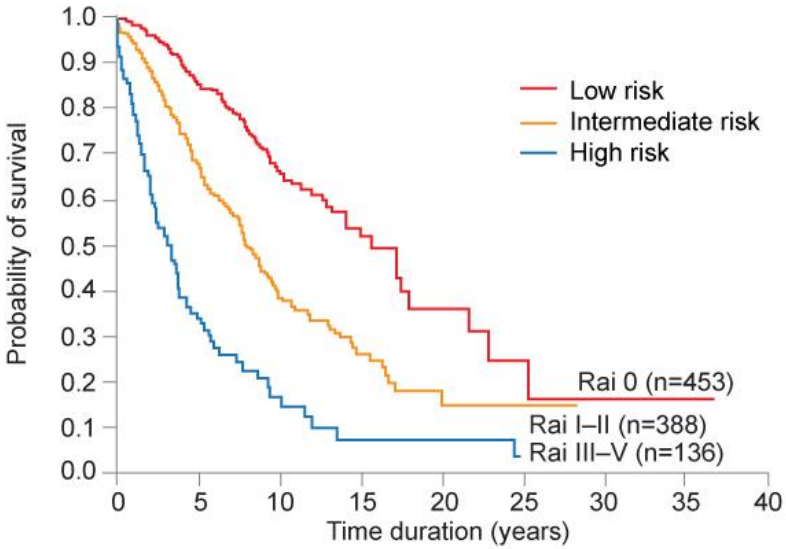
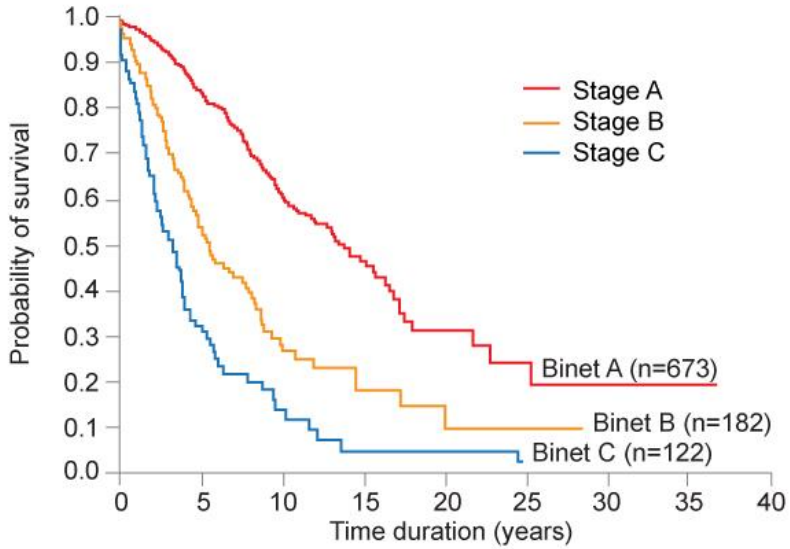
Prognostic value of staging systems

Rai system



Stage	Median survival (years)[5]
Low risk	~15 years
Intermediate risk	5–7 years
High risk	<3–4 years

Binet system



Stage	Median survival (years)[5]
Stage A	~15 years
Stage B	5–7 years
Stage C	<3–4 years

Redrawn from Montserrat et al 2006. Figures in the tables are estimations based on the curves above

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Prognostic factors

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Prognostic factors

Factors	Associated risks
Age	• Increasing age is an adverse prognostic factor[6]
Comorbidities	• Comorbidities determine the choice of treatment[7]
Lymphocyte doubling time (LDT)	• LDT <12 months is associated with a considerably decreased progression-free survival (PFS) and overall survival (OS)[8]
Cytogenetic abnormalities	• ~80% of people with CLL show cytogenetic abnormalities in their leukaemia cells • People with del(17p) mutation have the worst prognosis, followed by the del(11q) mutation, trisomy 12q, and normal diploid karyotype • Those with del(13q) mutation as a single abnormality have the best prognosis[9]
***IGHV* mutation status**	• People with *IGHV* mutations have a more favourable prognosis[12] • Those with unmutated *IGHV* may have higher genetic instability leading to more advanced and aggressive forms of the disease, and therefore a less favourable prognosis[12,13]
***TP53* mutation status**	• People with mutated *TP53* have a poorer prognosis[12]
Serum markers	• Serum markers that are associated with a poor prognosis include serum β2-microglobulin, serum thymidine kinase, and soluble CD23[10]
Karyotype	• Increased complexity of karyotype is associated with poor prognosis[11]

Summary

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Summary

Clinical staging

- The two widely used staging systems are the Rai and Binet systems
- The Rai system is mainly used in the United States and is based on organ involvement
- The Binet system is mainly used in Europe and is based on the number of areas of lymphadenopathy involved

Prognostic factors

Risk factors that influence a person's outcomes and course of treatment may include:

- Older age
- Comorbidities
- Low lymphocyte doubling time
- Cytogenetic abnormalities
- *IGHV* mutation status
- Distinct genetic features
- Distinct serum markers
- Complex karyotype

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Knowledge check

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Knowledge check: questions

1. In both the Rai and Binet staging systems, the presence of which of the following is an indicator that a patient is in the highest risk group?

A. Lymphocytosis
B. Thrombocytopenia
C. Anaemia
D. Splenomegaly

2. Which of the following factors is associated with a worse prognosis for patients with CLL?

A. Age <65 years
B. Increased lymphocyte doubling time
C. Unmutated *IGHV*
D. None of the above

3. Craig was recently diagnosed with CLL. His haemoglobin level is 9g/dL and his platelet levels are 80,000/μL. His spleen and groin are involved. Which Binet stage is his CLL?

A. Stage A
B. Stage B
C. Stage C

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Knowledge check: answers

1. **In both the Rai and Binet staging systems, the presence of which of the following is an indicator that a patient is in the highest risk group?**

   B: Thrombocytopenia (platelet levels <100,000/µL)

2. **Which of the following factors is associated with a worse prognosis for patients with CLL?**

   C: Unmutated *IGHV*

3. **Craig was recently diagnosed with CLL. His haemoglobin level is 9g/dL and his platelet levels are 80,000/µL. His spleen and groin are involved. Which Binet stage is his CLL?**

   C: Stage C

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