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## REVIEWER'S REPORT

Manuscript No.: IJAR-57411

Title: THE ROLE OF CONCURRENT RADIOTHERAPY-CHEMOTHERAPY IN THE MANAGEMENT OF UNOPERATED LOCALLY ADVANCED SQUAMOUS CELL CARCINOMAS OF THE LARYNX

### Recommendation:

Accept as it is .....

Accept after minor revision.....

**Accept after major revision .....YES**

Do not accept (*Reasons below*) .....

Rating	Excel.	Good	Fair	Poor
Originality		√		
Techn. Quality			√	
Clarity			√	
Significance		√		

Reviewer's ID: JPR-094

### Detailed Reviewer's Report

#### # \*\*Reviewer's Report\*\*

#### ## \*\*1. Summary of the Study\*\*

This manuscript evaluates the role of concurrent chemoradiotherapy (CCRT) in the management of inoperable locally advanced squamous cell carcinoma of the larynx through a 10-year retrospective study of 50 patients. It explores clinical characteristics, treatment modalities, toxicities, and outcomes, emphasizing larynx-preserving strategies.

#### ## \*\*2. Strengths\*\*

\* \*\*Relevant clinical topic:\*\* Addresses an important issue—organ preservation in advanced laryngeal cancer.

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- \* **Real-world data:** Provides insight from a decade-long institutional experience.
- \* **Comprehensive dataset:** Includes epidemiological, clinical, radiological, therapeutic, and toxicity data.
- \* **Multidisciplinary approach:** Highlights the role of tumor boards and supportive care.
- \* **Detailed radiotherapy description:** Clear explanation of GTV, CTV, PTV, and dosing protocols.
- \* **Focus on toxicity:** Both acute and late toxicities are documented, which is clinically valuable.

### ## 3. Weaknesses

#### \* Study design limitations:

- \* Retrospective and single-center → risk of bias.
- \* Small sample size (n=50) limits generalizability.
- \* **Lack of statistical analysis:**
  - \* No survival analysis (Kaplan–Meier curves missing).
  - \* No p-values, hazard ratios, or multivariate analysis.
- \* **Outcome reporting unclear:**
  - \* Overall survival (OS), progression-free survival (PFS), and laryngeal preservation rates not clearly quantified.
- \* **Selection bias:**

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- \* Only inoperable/refusal patients included—limits comparison with standard surgery.
- \* \*\*Inconsistent data presentation:\*\*
  
- \* Figures poorly integrated and sometimes unclear.
- \* Some duplication and formatting issues.
- \* \*\*Language and grammar issues:\*\*
  
- \* Numerous grammatical errors and awkward phrasing.
- \* Requires professional English editing.
- \* \*\*Literature discussion:\*\*
  
- \* Overly descriptive, lacks critical comparison with key trials (e.g., RTOG 91-11).
- \* \*\*Referencing issues:\*\*
  
- \* Inconsistent citation style.
- \* Some references outdated or duplicated.

### ## \*\*4. Key Points\*\*

- \* CCRT is widely used as a larynx-preserving strategy in locally advanced disease.
- \* Majority of patients were smokers and presented at advanced stages.
- \* Induction chemotherapy followed by CCRT was the most common approach.
- \* Significant acute toxicities (mucositis, dermatitis) were observed.
- \* Tumor response to induction chemotherapy was moderate (~51% >50% reduction).
- \* Multidisciplinary management is essential for optimal outcomes.

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### ## \*\*5. Significance of the Study\*\*

- \* Adds **regional data (Morocco)** to the global literature on laryngeal cancer.
- \* Reinforces the role of **CCRT** as a standard organ-preserving approach.
- \* Highlights **late presentation and risk factor burden** in developing settings.
- \* Provides insight into **treatment-related toxicities in real-world practice**.

However, the scientific impact is **moderate** due to methodological limitations and lack of robust statistical analysis.

### ## \*\*6. Recommendations (Major Revision)\*\*

#### ### **Major Issues to Address**

#### 1. **Statistical Analysis**

- \* Include survival analysis (Kaplan–Meier curves for OS and PFS).
- \* Provide statistical comparisons (p-values, confidence intervals).
- \* Consider multivariate analysis (prognostic factors).

#### 2. **Clarify Outcomes**

##### \* Clearly define:

- \* Overall survival (OS)
- \* Progression-free survival (PFS)
- \* Laryngeal preservation rate
- \* Add follow-up duration (median, range).

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### 3. **\*\*Improve Methodology Section\*\***

- \* Define endpoints explicitly.**
- \* Clarify inclusion/exclusion criteria.**
- \* Describe response evaluation criteria (RECIST?).**

### 4. **\*\*Revise Results Section\*\***

- \* Present data in structured tables.**
- \* Remove redundant narrative descriptions.**
- \* Improve figure quality and labeling.**

### 5. **\*\*Strengthen Discussion\*\***

- \* Compare findings with major trials (RTOG 91-11, MACH-NC).**
- \* Provide critical interpretation, not just description.**
- \* Discuss limitations clearly.**

### 6. **\*\*Language Editing\*\***

- \* Requires thorough proofreading by a native English speaker.**

### ### **\*\*Minor Issues\*\***

- \* Correct typographical and formatting errors.**
- \* Standardize references (e.g., Vancouver style).**
- \* Improve figure captions and numbering.**

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**\* Avoid repetition in introduction and discussion.**

**## \*\*7. Final Recommendation\*\***

**\*\*Major Revision Required\*\***

**The manuscript has clinical relevance but requires **\*\*substantial improvement in methodology, statistical rigor, and presentation\*\*** before it can be considered for publication in this peer-reviewed journal.**

**# **\*\*MAJOR REVISION JUSTIFICATION\*\*****

**## **\*\*1. Title & Abstract\*\*****

**\*\*Lines 1–3 (Title)\*\***

**\*  Issue: Title is too long and grammatically awkward (“UNOPERATED LOCALLY ADVANCED...”).**

**\*  “Concurrent radiotherapychemotherapy” phrasing is non-standard.**

**\*  Suggestion: Use standard term **\*\*Concurrent Chemoradiotherapy (CCRT)\*\***.**

**\*  Revise to:**

**“Role of Concurrent Chemoradiotherapy in Inoperable Locally Advanced Laryngeal Squamous Cell Carcinoma: A Retrospective Study”**

**\*\*Lines 7–18 (Abstract)\*\***

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\*  Issue: Abstract is **\*\*descriptive but not structured\*\*** (no Background, Methods, Results, Conclusion).

\*  Contains **\*\*general textbook statements\*\*** rather than study findings.

\*  Missing **\*\*key numerical outcomes\*\*** (response rate, survival, toxicity).

\*  No clear **\*\*study objective/hypothesis\*\***.

\*  Required: Structured abstract with:

\* Background

\* Methods

\* Results (with statistics)

\* Conclusion

### ## **\*\*2. Introduction\*\***

**\*\*Lines 21–40\*\***

\*  Issue: Too **\*\*generic and narrative\*\***, lacks strong research gap.

\*  Overuse of general knowledge instead of **\*\*recent literature (last 5 years)\*\***.

\*  No **\*\*clear objective or hypothesis statement\*\***.

\*  Add:

\* Clear **\*\*research gap\*\*** (e.g., lack of Moroccan data, outcome variability)

\* Explicit **\*\*study aim at end of introduction\*\***

### ## **\*\*3. Materials & Methods\*\***

**\*\*Lines 41–52\*\***

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\*  Issue: Study design described as “retrospective descriptive” but lacks rigor.

\*  Missing:

\* Sample size justification

\* Statistical analysis section

\* Definition of endpoints (OS, DFS, response criteria)

\*  Ethical statement is vague (no approval number).

\*  Must include:

\* Statistical tools (SPSS, p-values, CI)

\* Response criteria (RECIST?)

\* Toxicity grading (RTOG already used but not declared earlier)

### ## \*\*4. Results Section\*\*

\*\*Lines 53–258\*\*

### ### General Issues:

\*  Overly \*\*descriptive without statistical analysis\*\*

\*  No \*\*p-values, confidence intervals, or comparisons\*\*

\*  Excessive reliance on \*\*figures without interpretation\*\*

\*  Some inconsistencies:

\* Sex ratio (Line 55: 15.67 vs earlier 1.567)

\*  Poor formatting of figures (raw text, overlapping data)

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### ### Specific Issues:

#### **\*\*Lines 54–55\*\***

- \*  Inconsistent data (62.12 vs 62.16 years)

#### **\*\*Lines 56–59\*\***

- \*  Risk factor data lacks comparative/statistical significance

#### **\*\*Lines 68–90 (Figures)\*\***

- \*  Figures not properly labeled or referenced
- \*  No captions in journal format

#### **\*\*Lines 118–122 (TNM classification)\*\***

- \*  No staging system reference (AJCC edition missing)

#### **\*\*Lines 133–142 (Treatment)\*\***

- \*  No justification for regimen selection
- \*  No comparison between groups (induction vs direct CCRT)

#### **\*\*Lines 152–158 (Response evaluation)\*\***

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\*  Response criteria not defined

\*  No statistical significance

**\*\*Lines 159–164 (Toxicity)\*\***

\*  Toxicity not graded using a standardized scale in results (though later tables mention RTOG)

**\*\*Lines 203–207 (Radiotherapy dose)\*\***

\*  Dose description unclear and poorly formatted

**\*\*Lines 228–234 (Treatment protocol)\*\***

\*  Overly procedural (like textbook/manual, not research result)

**## \*\*5. Discussion\*\***

**\*\*Lines 259–524\*\***

**### Major Issues:**

\*  Discussion is **\*\*too long and unfocused\*\***

\*  Large portions are **\*\*textbookstyle review\*\***, not interpretation

\*  Poor linkage between **\*\*your results and literature\*\***

\*  No critical analysis of:

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\* Study limitations

\* Bias

\* Small sample size

### ### Specific Problems:

**\*\*Lines 259–267\*\***

\*  Repetition of epidemiology (already in introduction)

**\*\*Lines 274–293\*\***

\*  Excessive explanation of risk factors (not linked to study findings)

**\*\*Lines 386–408 (Historical treatment evolution)\*\***

\*  Too detailed; not directly relevant

**\*\*Lines 431–458 (Clinical trials discussion)\*\***

\*  Good content but not linked to your dataset

**\*\*Missing:\*\***

\*  Comparison of your survival (71.4%) with global studies

\*  Explanation of differences

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### ## **\*\*6. Conclusion\*\***

#### **\*\*Lines 525–534\*\***

- \*  **Too *\*\*general and descriptive\*\****
- \*  **Does not reflect *\*\*your actual study results\*\****
- \*  **Should include:**
  - \* **Key findings (response rate, toxicity, survival)**
  - \* **Clinical implication**
  - \* **Future recommendation**

### ## **\*\*7. References\*\***

#### **\*\*Lines 536–669\*\***

- \*  **Duplicate references (e.g., LerouxRobert appears twice)**
- \*  **Inconsistent formatting**
- \*  **Many *\*\*old references (>10-20 years)\*\****
- \*  **Missing DOI formatting**
- \*  **Must:**
  - \* **Follow journal style (Vancouver/APA)**
  - \* **Add *\*\*recent studies (2020–2025)\*\****

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### ## **\*\*8. Language & Formatting\*\***

- \*  **Frequent grammatical errors**
- \*  **Inconsistent terminology:**
  - \* **chemo radiotherapy / chemoradiotherapy / CCR**
- \*  **Formatting issues:**
  - \* **Tables not aligned**
  - \* **Figures embedded as raw text**
- \*  **Typographical errors:**
  - \* **“treatmentwasadministeredin”**
  - \* **spacing issues**

### # **\*\*Overall Major Revision Reasons\*\***

The manuscript requires **\*\*major revision\*\*** due to:

1.  **Lack of **\*\*statistical analysis and scientific rigor\*\*****
2.  **Poor **\*\*structure (abstract, methods, results)\*\*****
3.  **Overly **\*\*descriptive and not analytical\*\*****
4.  **Weak **\*\*link between results and discussion\*\*****
5.  **Formatting and language issues**
6.  **Missing **\*\*clear research contribution\*\*****

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#  **\*\*What You Should Do (Action Plan)\*\***

- \* Rewrite **abstract (structured)**\***
- \* Add **statistical analysis section**\***
- \* Include **p-values & comparisons**\***
- \* Shorten discussion (focus on your results)**
- \* Fix figures/tables professionally**
- \* Improve English (preferably proofreading)**
- \* Update references (recent + formatted)**