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DNA repair SNPs as biomarkers of therapeutic response in oral cancer patients: a systematic review

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Background:

Radiotherapy, chemotherapy, or their combination remain a mainstay in oral cancer treatment. Such agents introduce genetic lesions in tumour cells to kill them. Non-tumour cells are also affected, generating side effects, e.g., secondary cancers. DNA repair pathways exist that repair such therapy-induced genetic lesions and avoid their fixation as mutations (potentially oncogenic) or the activation of apoptosis. Since most DNA repair genes are polymorphic, with potential impact on enzyme expression or activity, patients carrying distinct genetic variants may have different capacity to repair genetic lesions. We conducted a systematic review to identify DNA repair SNPs that have been associated with altered response to radio or chemotherapy in the context of oral cancer and to characterize their impact on clinical outcome, therapeutic efficacy and safety.

Materials and methods:

- ✓ PRISMA guidelines
- ✓ PICO question: "Do DNA repair SNPs influence the clinical outcome of anticancer treatment in patients with oral cancer?"
- ✓ Databases searched: Pubmed, Web of Science
- ✓ MeSH term-based search expression: (Polymorphism, Single Nucleotide) AND ((DNA repair) OR (DNA repair enzymes)) AND ((mouth neoplasms) OR (Squamous Cell Carcinoma of Head and Neck)) AND ((drug therapy) OR (antineoplastic agents) OR (radiotherapy) OR (chemoradiotherapy)).

Results:

Database search identified 142 studies, 7 being compliant with selection criteria. Significant associations with overall survival, disease-free survival or therapeutic efficacy were observed for 3 BER, 4 NER, 2 MMR and 1 HR SNPs. The variant genotype of *MLH1* rs1800734 was negatively associated with overall survival and disease-free survival in two independent studies.

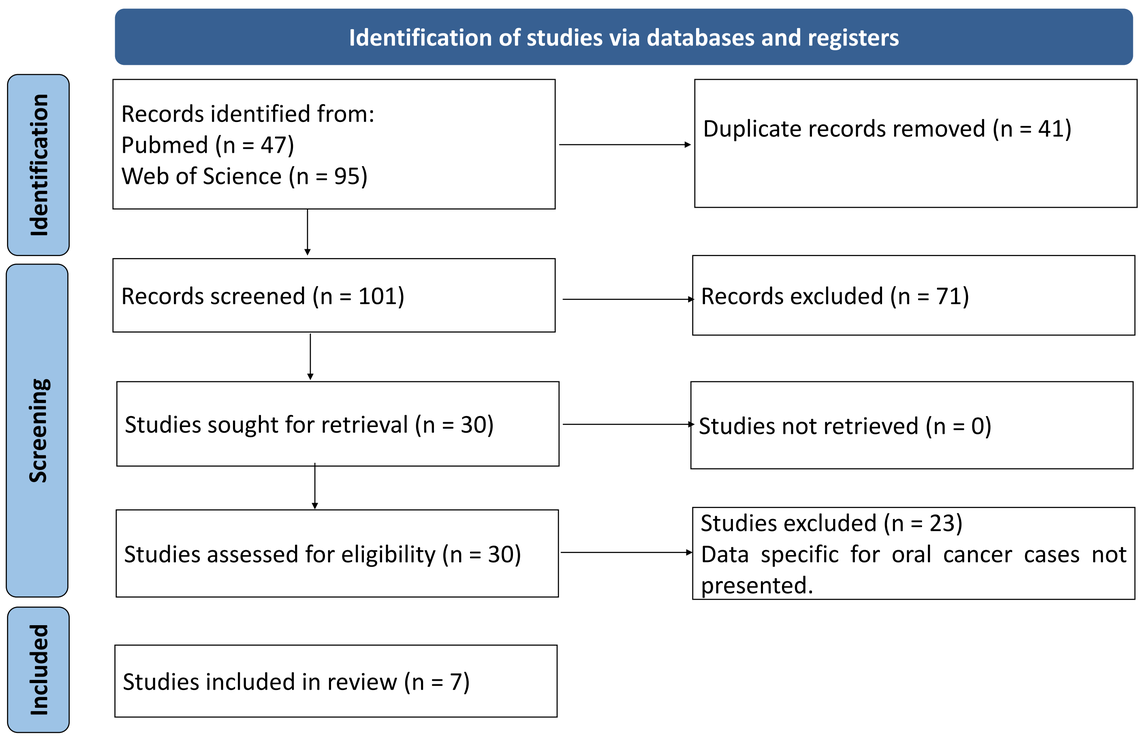

Figure 1: PRISMA flow diagram.

Table 1: Significant associations observed between DNA repair SNPs and overall survival (OS).

Gene	SNP	Alleles	Significant associations	Ref.
Base Excision Repair (BER)				
APEX1	rs1760944	T/G	GG genotype associated with worse OS.	[1]
XRCC1	rs1799782	C/T	CT+TT genotype associated with better OS.	[1]
Mismatch Repair (MMR)				
MLH1	**rs1800734**	**G/A**	**AA genotype associated with worse OS.**	**[2]**
MLH1	rs1800734	A/G	--	[3]

Table 2: Significant associations observed between DNA repair SNPs and disease-free survival (DFS).

Gene	SNP	Alleles	Significant associations	Ref.
Base Excision Repair (BER)				
MUTYH	rs3219489	C/G	G allele associated with worse DFS (increased recurrence risk).	[1]
Nucleotide Excision Repair (NER)				
ERCC1	rs735482	A/C	CC genotype associated with worse DFS (increased recurrence risk).	[4]
ERCC5	rs17655	G/C	CC genotype associated with worse DFS (increased recurrence risk).	[4]
Mismatch Repair (MMR)				
MLH1	**rs1800734**	**G/A**	**AA genotype associated with worse DFS (increased recurrence risk).**	**[2]**
MLH1	**rs1800734**	**A/G**	**GG genotype associated with better DFS (decreased recurrence risk).**	**[3]**
MSH2	rs3732183	A/G	GG genotype associated with better DFS (decreased recurrence risk).	[3]
Homologous Recombination (HR)				
XRCC2	rs2040639	G/A	A allele associated with better DFS (decreased recurrence risk).	[5]

Table 3: Significant associations observed between DNA repair SNPs and chemotherapy efficacy.

Gene	SNP	Alleles	Significant associations	Ref.
Nucleotide Excision Repair (NER)				
ERCC1	rs11615	C/T	CC and CT genotypes associated with better response to chemotherapy.	[6]
ERCC1	rs11615	C/T	--	[7]
ERCC1	rs3212986	C/A	CC genotype associated with better response to chemotherapy.	[6]

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Conclusions:

MLH1 rs1800734 may influence the clinical outcome of radio and/or chemotherapy in oral cancer patients. Further studies are needed to validate these results. Deepening such knowledge could help to individualize the treatment strategy according to the patient's genetic profile, thus improving clinical outcome in these patients.

SCAN ME

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