Quality of life and functional capacity in patients with rheumatoid arthritis – Cross-sectional study

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A R T I C L E   I N F O

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A B S T R A C T

Objectives: To analyze the Health related Quality of Life (HRQoL) and physical function in rheumatoid arthritis (RA) patients and compare it with the general population. We also intended to analyze about disease activity influence in HRQol and functional capacity, as well as determine potential determinants for these outcomes.

Material and methods: A cross-sectional study was conducted in RA patients from a university hospital of Portugal. We obtained Short Form 36, EuroQol 5D, health assessment questionnaire, visual analog scale for pain and patient’s assessment of disease activity. Comparisons between SF-36 and EQ-5D values with our population reference values were conducted using the Mann–Whitney test. Data were compared in different levels of disease activity, using Kruskal Wallis test and Fisher's exact test. A multiple regression analysis was conducted to identify the potential determinants of outcomes.

Results: RA sample showed significantly lower values than the portuguese general population on physical summary measure of SF-36 (median = 32 vs. 50, p < 0.001) and EQ-5D (median = 0.620 vs. 0.758 respectively; p < 0.001). Lower disease activity levels had better PROs and this was true even when compared patients achieving remission with those in low disease activity. The HAQ ($r^2 = 67\%$), VAS-P ($r^2 = 62\%$) and VAS-DA ($r^2 = 58\%$) were the variables that strongly related to SF-36. Considering HAQ, the strongest relation was found with VAS-P, VAS-DA and age ($r^2 = 60\%, 61\%$ and $33\%$, respectively). Multiple regression analysis identified HAQ, VAS-P and educational status as determinants of the HRQol; age, female gender, employment, VAS-P and VAS-DA as determinants of physical function.

Conclusion: Impairment of HRQol in RA patients is enormous. We found significant differences between different levels of disease activity, showing higher HRQol and functional capacity at lower disease activity levels.

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R E S U M E N

Objetivos: Analizar la evaluación del Health related Quality of Life (HRQoL) y la función física en pacientes con artritis reumatoide (AR) y compararla con la población general. También se pretende analizar la influencia de la actividad de la enfermedad en el HRQol y la capacidad funcional, así como definir los determinantes potenciales de estos resultados.

Material y métodos: Se realizó un estudio transversal en pacientes con AR de un hospital universitario de Portugal. Se obtuvieron los cuestionarios Short Form 36, EuroQol 5D, Health Assessment Questionnaire,

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la escala analógica visual de dolor y la evaluación de la actividad de la enfermedad. Las comparaciones entre los valores de SF-36 y EQ-5D con los valores de referencia de nuestra población se condujeron utilizando el test de Mann-Whitney. Los datos se compararon en diferentes niveles de actividad de la enfermedad utilizando el test de Kruskal Wallis y la prueba exacta de Fisher. Se realizó un análisis de regresión múltiple para identificar los determinantes potenciales de los resultados.

**Results:** La muestra de AR mostró valores significativamente más bajos que la población general portuguesa en la medición física de SF-36 (mediana = 32 vs. 50, p < 0.001) y EQ-5D (mediana = 0.620 vs. 0.758, respectivamente, p < 0.001). Los pacientes con niveles de actividad de la enfermedad más bajos tuvieron mejores PRO y esto fue cierto incluso cuando se compararon los pacientes que alcanzaron la remisión con aquellos en baja actividad de la enfermedad. El HAQ (r² = 67%) y VAS-DA (r² = 62%) y VAS-DA (r² = 58%) fueron las variables fuertemente relacionadas con SF-36. Con respecto al HAQ, se encontró una relación más fuerte con VAS-DA y la edad (r² = 60%, el 61 y el 33%, respectivamente). El análisis de regresión múltiple identificó el HAQ, el VAS-DA y el nivel de estudios como determinantes del HRQol y la edad, el género femenino, el empleo, VAS-P y VAS-DA como determinantes de la función física.

**Conclusión:** El deterioro del HRQol en los pacientes con AR es enorme. Se encontraron diferencias significativas entre diferentes niveles de actividad de la enfermedad, mostrando mayor HRQol y capacidad funcional en niveles más bajos de actividad de la enfermedad.
index value for health status. The five dimensions included in the EQ-5D are: mobility; self-care; usual activities; pain/discomfort and anxiety/depression. Each dimension has three levels (none, some or major problems) and together defines 243 health states (3 to the power of 5 gives the 243 possible combination), to which has been added “unconscious” and “dead” for a total of 245 health states. EQ-5D scores range between −0.594 and 1 (full health).

Limitations in activities of daily life were assessed by Portuguese version of the Health Assessment Questionaire (HAQ), which comprises eight categories. A score of 0 (no difficulty), 1 (some difficulty), 2 (much difficulty or need of assistance) or 3 (unable to perform) is given to each question; the highest score in each category represents the score for that category. The sum of scores is then divided by the number of categories, yielding a total score ranging from 0 (best) to 3 (worst).

Visual Analog Scales (VASs) were used, on which patients had to indicate on a scale from 0 (none) to 100 (worst) mm their rating of disease activity (VAS-DA) and pain (VAS-P).

Data collection

Data collection was performed in the rheumatology day-care hospital unit and through the longitudinal national database “reuma.pt”. The collected variables were C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), numbers of swollen and tender joints by using a 28-joint count (SJC28, TJC28); VAS-P and VAS-DA, and HAQ. Composite indices, such as the simplified disease activity indice (SDAI) and the Disease Activity Score using 28-joint counts (DAS28-4V) were calculated by informatic system. Age, gender, level of education, marital and employment status as well as additional disease characteristics – disease duration, rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibody (anti-ACCP) status, extra-articular manifestations (rheumatoid nodules, ocular, rheumatoid vasculites and pleuropulmonary) and DMARDs use – were also recorded. The application of questionnaires, available in the computer system, was held through face-to-face interviews.

Statistical analyses

In the description of socio-demographic and clinical characteristics as well as in the description of PROs (eight domains of SF-36, PSM, MSM, EQ-5D, HAQ, VAS) were used means and standard deviations for continuous variables with symmetrical distribution and median and range (minimum and maximum) for the variables continuous with asymmetric distribution. Categorical variables were expressed as proportions. To compare HRQoL of our RA patients to that of the portuguese general population, we used SF-36 published data by Ferreira et al. Measures of central tendency were compared using the Mann–Whitney test. To investigate whether outcomes are different at different levels of disease activity we divided sample according to level of disease activity by SDAI: remission (REM) SDAI < 3.3, low disease activity (LDA) 3.3 < SDAI < 11, moderate disease activity (MDA) 11 < SDAI < 26 and high disease activity (HDA) SDAI > 26. The comparison of outcomes was performed using Kruskal Wallis test and Fisher’s exact test, for medians and categorical variables, respectively. To assess the relationship between clinical data and the PROs, Spearman correlations (ρ) were performed. To identify explanatory variables of HRQoL and functional capacity we conducted a multiple linear regression (stepwise selection) and included variables statistically significant in univariate analysis and those considered clinically relevant. We assessed correlations between the continuous variables and HRQoL with Spearman correlation to check for collinearity. Linear regression model assumptions were examined and satisfied. Residual plots were examined for goodness of fit. Analyses were performed using the program SPSS Version 21. The p-values below 0.05 were considered significant.

Results

Socio-demographic, clinical and laboratory characteristics are documented in Table 1. At the moment of this study we found that 8.4% (n = 13) were in REM, 53.2% (n = 82) had LDA, 33.8% (n = 52) had MDA and 4.5% (n = 7) had HDA. Most patients (n = 107) were under the first biological agent and the median time under the drug was 6 years (range 0–10). Eight patients (5.2%) were under the current drug for 10 years and 27 (17.5%) for 2 years or less.

HRQoL and functional status of RA patients

After analysing all domains of the SF-36 we observed that the domain with lowest score was the “Physical Performance” (median 25) followed by the domain “General Health” and “Physical Functioning” (median 40 for both). Mental domains showed higher values; among them, domain “Social Functioning” showed the lowest score (median 40; range 3–53). The domain “Role-Emotional” had a median of 100 (range 0–100) (Table 2).

Likewise, we found that in SF-36 summary measure, PSM was lower than MSM (median 32 vs. 52). With the application of EQ-5D also observed a low score (median 0.620, range –0.349 to 1.000). In our sample, 5% of patients (n = 6) had scores on the EQ-5D less than zero (states worse than dead). Median score was 1.250 (range 0.000–2.875) for HAQ (Table 2).

When comparing primary outcomes between genders we found significant statistical differences only for the HAQ in which woman
Table 2
Patient-reported outcomes (PRO).

<table>
<thead>
<tr>
<th>Sample (n = 154)</th>
<th>REM (n = 13)</th>
<th>LDA (n = 82)</th>
<th>MDA (n = 52)</th>
<th>HDA (n = 7)</th>
<th>p Value between REM and LDA*</th>
<th>p Value between all groups**</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS-P 50 (0–100)</td>
<td>6 (0–30)</td>
<td>32.5 (0–95)</td>
<td>60 (0–100)</td>
<td>70 (50–100)</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>VAS-GH 50 (0–100)</td>
<td>0 (0–20)</td>
<td>40 (0–80)</td>
<td>60 (20–100)</td>
<td>70 (50–100)</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>HAQ 1.25 (0.00–2.88)</td>
<td>0.50 (0.00–1.13)</td>
<td>1.13 (0.00–2.75)</td>
<td>1.63 (0.38–2.88)</td>
<td>2.00 (1.13–2.75)</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>EQ-5D 0.620 (–0.349–1.000)</td>
<td>0.848 (0.708–1.000)</td>
<td>0.673 (–0.349–1.000)</td>
<td>0.516 (–0.349–0.812)</td>
<td>0.516 (0.053–0.760)</td>
<td>0.001</td>
<td>0.001</td>
</tr>
</tbody>
</table>

SF-36: PH
PF 40 (0–100) 75 (45–95) 40 (0–100) 30 (5–70) 30 (5–60) 0.001 0.001
PRF 25 (0–100) 100 (0–100) 50 (0–100) 25 (0–100) 0 (0–75) 0.002 0.001
BP 51 (0–100) 84 (10–100) 52 (0–100) 41 (0–80) 12 (10–62) 0.011 0.001
GHP 40 (0–72) 45 (35–72) 40 (10–72) 35 (15–65) 35 (5–50) 0.020 0.009

SF-36: MH
VT 50 (20–70) 50 (40–55) 50 (20–70) 50 (30–60) 45 (45–55) 0.655 0.815
SRF 40 (3–53) 51 (28–52) 40 (13–53) 40 (3–53) 51 (15–53) 0.118 0.153
ERF 100 (0–100) 100 (0–100) 100 (0–100) 67 (0–100) 100 (0–100) 0.023 0.054
MH 52 (0–100) 84 (28–50) 56 (0–100) 44 (4–100) 44 (32–72) 0.004 0.001
PSM 32 (14–66) 54 (18–62) 37 (15–65) 24 (14–53) 20 (14–45) 0.001 0.001
MSM 52 (23–69) 51 (33–64) 52 (23–66) 51 (36–69) 53 (43–65) 0.820 0.839

VAS-P, visual analog scales of pain; VAS-GH, visual analog scale for general health; HAQ, Health Assessment Questionnaire; EQ-5D, EuroQol five dimensions questionnaire; SF-36, Short Form Health Survey; PH, physical health; PRF, physical role functioning; BP, bodily pain; GHP, general health perceptions; VT, vitality, SRF, social role functioning; ERF, emotional role function; MH, mental health; PSM, physical summary measures; MSM, mental summary measures.

Values presented as medians (range). *P-value between different groups of disease activity by “Mann-Whitney and ** Kruskal-Wallis test.

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Fig. 1. Comparison of SF-36 values of RA patients with general Portuguese population. Significant differences of different domains of SF-36 was found (p < 0.001 for all analyses, except emotional role functioning (p = 0.079), p-value using Mann–Whitney test.

Comparison of HRQoL of RA patients with general Portuguese population

HRQoL of our RA patients is lower than the general Portuguese population. Our patients had significantly lower scores in all domains of the SF-36, except for “Emotional role functioning” (Fig. 1), Regarding summary measures there is a significant difference in MSF (median 32 vs. 50, p < 0.001) but not in the MSM (median 50 vs. 52, p = 0.503). The same was observed through EQ-5D in which our patients had lower median score than general Portuguese population (0.620 vs. 0.758, p < 0.001). Comparing the presented worse results (median 1.38 vs. 0.88; p = 0.024). There were no significant differences in PROs when evaluated according to disease duration (< 10 or > 10 years), RF and ACCP status, presence of extra-articular manifestations or current biological therapy.

HRQoL of general Portuguese population with our patients in clinical remission, we found similar scores for the several individual domains and the summary measures of SF-36 (Fig. 2).

Regarding EQ-5D values, we also found identical values between REM group and the general population (0.848 vs. 0.758).

HRQoL and functional disability correlate significantly with disease-activity levels

The performed analysis by disease activity groups showed significant differences in all applied instruments (Table 2).

When we access the functional capacity using the domains of physical health of the SF-36 (PF, PRF, BP and GHP) we also found statistically significant difference, showing worst scores with highest disease activity (p < 0.001 for all analyzers). For the SF-36 mental health domains we only observed progressive decrease in the score with increase of level of activity disease on the “mental health” domain (p = 0.001) (Table 2 and Fig. 3). The same was true for
the SF-36 summary measures, i.e., decreasing scores of PSM with increasing levels of disease activity ($p < 0.001$) and overlapping MSM values (Table 2). When we assessed potential differences in HRQoL by other measures, such as EQ-5D, we found very similar results ($p < 0.001$) (Table 2).

Comparing functional disability by HAQ at the four levels of disease activity, we observed significant differences between groups, showing a HAQ increase with increasing disease activity ($p < 0.001$) (Table 2).

In order to compare the benefit of remission with state of low disease activity with respect to the PRO we directly compared REM group with LDA (Table 2). In this analysis we observed a statistically significant difference in all PRO (SF-36, EQ-5D, HAQ, and VAS) except in “Vitality” and “Social role functioning” domains and mental summary measure of the SF-36.

HRQoL and functional disability have a weak correlation with clinical and laboratory data

We evaluated the relationship between the various clinical and laboratory parameters with the PRO through the Spearman correlation ($\rho$).

The analyzed clinical and laboratory variables were: current age and age at disease onset, disease duration, education level, CRP, ESR, tender and swollen 28-joint count, DAS28 change, VAS-P and VAS-GH. We also studied the relationship between the PSM of SF-36 and initial and actual HAQ.

For PSM we concluded that variables with strongest relationship were those that correspond to other PRO, namely current and initial HAQ ($\rho = −0.67$ and $−0.48$, respectively), VAS-P ($\rho = −0.62$) and VAS-GH ($\rho = −0.58$) ($p < 0.001$ for all analyses). The relationship with tender and swollen 28-joint count, although significant, was much lower ($\rho = −0.35$ and $−0.20$, respectively). There was no correlation with ESR ($\rho = 0.02$, $p = 0.84$) nor with CRP ($\rho = 0.07$, $p = 0.365$). For MSM no significant correlations were identified.

The HAQ also showed weak correlation with ESR, CRP and 28-joint count. The strongest correlations were observed with PSM of SF-36 ($\rho = 0.674$), VAS-GH ($\rho = 0.609$), VAS-P ($\rho = 0.601$) and initial HAQ ($\rho = 0.595$) ($p < 0.001$ for all analyzes).

### Table 3

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient $\beta$</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Higher education</td>
<td>3.887 $^{**}$</td>
<td>0.424–7.350</td>
</tr>
<tr>
<td>Higher HAQ</td>
<td>$−9.191^*$</td>
<td>$−11.788$ to $−6.451$</td>
</tr>
<tr>
<td>Higher VAS-P</td>
<td>$−0.165^*$</td>
<td>$−0.233$ to $−0.097$</td>
</tr>
<tr>
<td>$R^2$ (%)</td>
<td>54.6</td>
<td></td>
</tr>
<tr>
<td>MSM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$R^2$ (%)</td>
<td>$−$</td>
<td></td>
</tr>
<tr>
<td>EQ-5D</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Higher HAQ</td>
<td>$−0.208^*$</td>
<td></td>
</tr>
<tr>
<td>Higher VAS-GH</td>
<td>$−0.003^*$</td>
<td>$−0.271$ to $−0.145$</td>
</tr>
<tr>
<td>$R^2$ (%)</td>
<td>46.4</td>
<td>$−0.005$ to $−0.001$</td>
</tr>
<tr>
<td>HAQ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Higher age</td>
<td>0.011 $^{***}$</td>
<td>0.003–0.018</td>
</tr>
<tr>
<td>Female gender</td>
<td>0.247 $^{**}$</td>
<td>0.014–0.480</td>
</tr>
<tr>
<td>Current employment</td>
<td>$−0.313^*$</td>
<td>$−0.484$ to $−0.141$</td>
</tr>
<tr>
<td>Higher VAS-GH</td>
<td>0.010</td>
<td>0.004–0.016</td>
</tr>
<tr>
<td>Higher VAS-P</td>
<td>0.006</td>
<td>0.001–0.011</td>
</tr>
</tbody>
</table>

PSM, physical summary measures; HAQ, Health Assessment Questionnaire; VAS-P, visual analog scales of pain; MSM, mental summary measures; EQ-5D, EuroQol five dimensions questionnaire; VAS-GH, visual analog scale for general health.

Again, we verified that variables with strongest correlation with EQ-5D were other PRO (VAS-GH $\rho = −0.573$ and VAS-P $\rho = −0.560$, $p < 0.001$ for both) and not the clinical or laboratory classics data. There was not a significant association between the SF-36, EQ-5D and HAQ with the variation of DAS28-4V.

### Determinants of HRQoL

The potential explanatory variables considered for summary measures of the SF-36, EQ-5D and HAQ were age, gender, level of education, employment status, disease duration, VAS-GH, VAS-P, tender and swollen 28-joint count, ESR, CRP and DAS28-4V change. For SF-36 and EQ-5D we also included HAQ questionnaire. The regression coefficients are documented in Table 3. HAQ, VAS-P and level of education were retained as explanatory variables for PSM. The explained variance ($R^2$) was $85\%$ ($p < 0.001$) and HAQ had the stronger effect on PSM ($\beta = −9.119$, $p < 0.001$). For MSM, the model has not retained any significant explanatory variable. Therefore, we found no demographic or clinical variable to explain mental health. HAQ and VAS-GH were retained as explanatory variables for EQ-5D and the model’s explanation of the variance was significant (46.4%). As observed for PSM, HAQ was the variable with stronger effect on the EQ-5D ($\beta = −0.208$, $p < 0.001$).

Studying HAQ determinants, we found that higher age, female gender, current employment, VAS-P and VAS-GH explained 50% of the variation. Presence of current employment was the variable with the greatest impact on functional capacity ($\beta = −0.313$).

Clinical and laboratory classic data (joint count, acute-phase reactants and DAS28-4V change) showed no explanatory effect on HRQoL and functional capacity of these patients.

### Discussion

The present study provides information on the effect of RA on HRQoL and functional capacity, in a real world setting. Our results corroborate previous studies showing that patients with RA had not only significant physical function and mental...
health impairment but also poor HRQoL when compared to general Portuguese population. Differences are particularly notable on physical domains of SF-36 however, RA patients also present levels of mental health subscales significantly lower than general population.

In our study we verified values of EQ-5D corresponding to states of “full health”. Several factors may explain this finding. One of the disadvantages of the EQ5D is that may suffer from ceiling effect. The questionnaire is not sensitive enough to discriminate between different levels of health because the dimensions are probably not sufficiently disaggregated, leading individuals to respond at the highest level. These finding may indicate that individuals with significant morbidity are misclassified as in full health on the EQ-5D descriptive system.

When we evaluated disease activity influence in HRQoL and functional capacity, we found significant negative correlation (HRQoL and functional impairment with higher disease activity levels). A interesting finding in our study was to note a stronger correlation between SF-36 and measures of disability and pain (HAQ and VAS-P) than with measures directly related to disease process (ESR, CRP, joint count). Another finding was the benefit found in these outcomes when REM status was compared directly with LDA. Thus, indicators of quality of life, functional capacity, pain and appreciation of global health patient-reported complementing the clinical evaluation.

With regard to the potential determinants of these outcomes, we verified that older age and female gender was associated with higher HAQ score. This data confirms previous results. Physical function declines with age and it is known that women have lower threshold for pain and that men have more physical strength than women. Current employment was also related to better HAQ scores.

With regard to HRQoL, we identified higher education level and functional capacity as potential determinants.

Unlike other results, the duration of disease showed no significant linear relationship with none of the outcomes.

Several limitations of our study should be addressed. We studied a non-representative sample of the Portuguese population. Although the sample was from a reference center of Portugal, this is a convenience sample and the sample size is potentially small. This is a cross-sectional analyses; therefore, prevents to establish directionality of interpretation, i.e., unknown if group of patients in remission and low disease activity showed better SF-36, EQ-5D and HAQ when presented higher levels of disease activity. Other limitation is the fact that the joint damage was not assessed. This becomes relevant for two reasons. We observed that most patients studied have disease for over 10 years and we know that in late disease the functional capacity is most associated with joint damage.

The other reason is when we compare our sample with general population and observed that although all domains that compose the FSM were significantly lower, the difference is more pronounced for “physical functioning” and “physical role functioning” domains than for the “bodily pain” domain. Many patients with inactive disease but with important damage have functional limitations but do not refer pain complaints. Finally, the Portuguese population used to compare the HRQoL presents some characteristics that may affect the validity of the results. About 40% of the people interviewed report some type of pathology (namely musculoskeletal). However, this data has not been clinically confirmed based solely on patient-reported. Data such as gender and age were similar. Most were female and were between 30 and 69 years of age. In this way, we believe that there was no great influence on the results.

Strengths of the present analyses were the inclusion of a sample of patients with a broad range of clinical characteristics, rather than the more homogeneous populations of the trials; the focus on the more-stringent SDAI remission criteria, which allowed the recognition of the differences between REM and all other states, including LDA; it addressed quality of life not only through the state of health (SF-36) but also by assessing the value of health (EQ-5D) reported by the patient. The fact that it included the utility measure will enable future cost-effectiveness studies. Finally, analysis of summary measures of SF-36 as well as each of the domains provides a clearer picture of the dimensions affected by the disease.

We consider our results useful to better understand the impact of disease and establish a basis for future prospective studies with larger samples to assess the efficacy of therapeutic interventions. The focus on seriously ill patients in need of costly therapy may also be useful for cost-utility analysis studies of biotech drugs.

Conclusion

RA has considerable impact on quality of life and functional capacity being the impairment of HRQoL enormous when compared to general population. We verified lower HRQoL and functional capacity with higher disease activity levels and we saw that reaching remission seems to be a desirable state also from patient perspective. Since the clinical and laboratory data are weakly correlated with HRQoL and functional capacity, we believe that access to PROs is very important in order to complete the disease assessment.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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Authors contributions

All authors make substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data. All critically revise it for important critical content and give final approval of the version of the article accepted for publication.

Conflicts of interest

None of the authors has any conflicts of interest to declare.

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References


