Health status and disease burden of patients with psoriatic arthritis in Hungary

Ph.D. Thesis

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1 Introduction

Psoriatic arthritis (PsA) is a chronic inflammatory arthritis associated with psoriasis. PsA is characterized by asymmetrical peripheral (oligoarticular or polyarticular) joint inflammation and/or axial involvement (sacroileitis, spondylitis). Among small joints, interphalangeal, carpal and tarsal articulations of the hands and feet are often affected.

In chronic diseases it is crucial to be aware of the disease course, progression, health status and quality of life changes and to measure the effects of the therapies by standardized methods. In Hungary, a comprehensive use of such measures did not spread widely in the field of PsA. Only partial information is available about the PsA patients' clinical status, quality of life, the therapies applied and the disease related costs.

In the past years biological drugs have received coverage for the treatment of PsA. In view of their high costs, cost-of-illness studies and cost-effectiveness analysis have become into focus. In Hungary, health economic analysis is required for reimbursement decision of a new drug. Country-specific input data on quality of life and disease related costs are needed for appropriate cost-effectiveness analysis.

2 Objectives

1. Our aim was to assess the health status of PsA patients in Hungary:
   1.1. Analysis of patients' health status and health related quality of life, considering disease activity, functional status and characteristics of health care utilization

1.2. Comparison of PsA patients' quality of life with rheumatoid arthritis (RA) and general population in Hungary
1.3. To study the determinant factors of health status in PsA

2. To assess the PsA related costs in Hungary:
2.1. Survey of the PsA related costs and analysis of cost drivers
2.2. Comparison of diseases related costs of PsA with RA
2.3. Matching our cost-of-illness results with other European countries

3 Methods

From December 2007 to March 2008 a cross-sectional, retrospective questionnaire survey of 183 consecutive patients aged ≥18 years with established diagnosis of PsA was conducted in 8 rheumatology outpatient centres based on hospital in Hungary.

Disease activity (Disease Activity Score 28 (DAS28) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)) were assessed. Patients filled in the validated Hungarian version of the Health Assessment Questionnaire (HAQ), EQ-5D, the Psoriatic Arthritis Quality of Life Questionnaire (PsAQoL) and the EuroQoL (EQ-5D). Data were collected on the healthcare resource consumption in the past one year. Using the generic EQ-5D, health status of the PsA patients was compared to age-matched RA patients from a similar survey in 2004, and also to the results of a representative survey among the general Hungarian population. Relationship between health status, disease activity and quality of life was analyzed.

Cost calculation was performed based on survey data assessing one year time horizon. Both joint related and skin related costs were considered. Cost

calculation was performed in societal perspective, that means besides medical costs and non-medical direct costs, costs of productivity loss were also taken into account. Unit costs were based on the prices from year 2007.

Costs were divided into three main categories: direct medical costs (drug, diagnostic, medical aid, hospitalization, general practitioner visit and specialist visit), direct non-medical costs (home remodelling, transportation and informal care) and indirect costs (sick leave and productivity loss due to disability pension). Both human capital and friction cost methods were adopted when indirect costs were calculated.

Unit costs were determined using the databases of the Health Ministry, the National Health Insurance Found Administration, the Hungarian Central Statistical Office and the National Institute for Strategic Health Research. First the unit costs of the different resources were calculated; secondly unit costs were multiplied with the number of utilizations, after all the yearly costs were summed at each patient and mean annual cost was calculated.
A systematic literature search (until February 2009) was conducted to identify the published cost-of-illness studies in PsA and our results were compared to the international data.

Data were analysed using the Statistical Package of Social Sciences, version 14.0. Comparisons of variables between categories were performed using analysis of variance. The levels of significance were set to 95%.

4 Results

4.1 Basic characteristics

A total of 183 PsA patients were enrolled in the study, of these, 104 (57%) were women. The mean age of the sample was 50.1 (SD 12.9) years and the mean disease duration was 9.2 (SD 9.2) years. The main health status variables were as fallows the DAS28 4.4 (1.7), the BASDAI 45.7 (22.5), the HAQ 1.0 (0.79), the EQ-5D 0.47 (0.35) and the PsAQoL 7.7 (6.0). Patients had cutaneous manifestation for an average of 10 years before the onset of PsA.

The most frequent joint localization was the axial form (52%) and the rarest localization was the arthritis mutilans (7%). When axial joints were involved both the physicians and the patients assessed the global health status (measured by visual analouge scale (VAS)) and the health related quality of life (PsAQoL) was worse.

4.2 Health related quality of life

Quality of life (EQ-5D) in patients with PsA and RA was compared. There was no significant difference between the two diseases. The quality of life in patients with PsA in the age group 45-54 years was significantly worse (P=0.04) than in patients with RA in similar age. The differences were neither significant nor tendentious in the other age groups.

PsA patients' quality of life was lower compared to the general Hungarian population in each age group. In our sample 7.7 % of the patients' quality of life can be categorized as very good or good. Both the generic EQ-5D and disease specific PsAQoL were in strong correlations with the HAQ score (R=0,681 and

R=0,619). Also the disease activity measures the DAS28 and the BASDAI correlated strongly with the generic (EQ-5D) (R=-0,462 and R=-0,653) and with disease specific (PsAQoL) (R=0,460 and R=0,433) quality of life.

4.3 Health care resource use

Almost half of the patients (50.3%) got some kind of disease-modifying antirheumatic drugs. Of them 11 patients (6%) got biologic therapy, 8 patients for cutaneous manifestation and 3 patients for PsA. Thirty two percentages of patients used some devices (locomotion aids, therapeutic appliances) in the past one year. The numbers of patients with at least one visit at general practitioner or specialists or admission to hospital were 103 (56.3%), 155 (84.7%) és 77 (42.1%), respectively.

4.4 Costs

In our sample the annual mean (SD) total costs were 1 400 000 (1 888 000) HUF/patients/year in 2007. The cost domain with the biggest share was the productivity loss due to disability pension (49.2%), which was followed by the costs of biologic therapies (18.1%). The annual mean direct and indirect costs were 469 000 and 726 000 HUF/patients/year with 33.7% and 52.1% share respectively. Mean indirect costs were 48 000 HUF/patients/year when friction costs method was applied, in this case the total costs were 716 000 HUF/patients/year

Age, gender, level of education and martial status had no significant impact on total and direct medical costs (P>0.05). The age at onset of PsA and the total and direct medical costs correlated well, i.e. earlier onset occurs higher costs.

The costs were affected by the localization of arthritis in our study. Patients with symmetric polyarthritis had higher average total costs than patients without polyarthritis, the difference was 568 000 HUF (P=0.044). Patients with mono- or oligoarthritis had significantly lower total and direct medical costs than patients with any other type of arthritis. According to our estimation one point increase of the HAQ score resulted in 60 000 HUF increase in the direct medical costs. The disease activity measures, the DAS28 and the BASDAI correlated well with the total costs, worth activity was accompanied by higher costs.

4.5 Comparison of costs with RA

Costs of RA were higher in all domains than of PsA. The distribution of costs between cost categories was similar in the two diseases. The highest difference was observed at the direct medical costs where costs were elevated by 78% in RA. Indirect costs were higher by 47% in RA.

4.6 Comparison of costs with international data

Our literature search identified only one cost-of-illness study from Germany. The results of this German study were based on the national registry of rheumatology centres. The German costs were changed to HUF and were adjusted by the inflation. Costs of PsA were lower in each category in Hungary

than in Germany. The average annual direct, indirect and total costs were lower by 538 000, 2 235 000 and 2 773 000 HUF lower in Hungary.

5 Conclusions

Observations drawn from our study:

1. Health status and quality of life of PsA patients
   - 1.1. Disease burden of PsA is substantial. There is about a 10 years interval between the first skin symptoms and establishment of PsA diagnosis. Therefore, rheumatic complaints of patients with psoriasis should be especially considered and presence of PsA should be monitored. Spine symptoms are of special interest and revealing axial involvement is crucial as it significantly worsens patients' quality of life.
   - 1.2. Quality of life is seriously affected in the majority of the patients. Health status (EQ-5D) of the PsA patients is comparable to rheumatoid arthritis in all age-groups and it is significantly worse than of the general population.
   - 1.3. Functional status and disease-activity is in strong correlation with generic and disease-specific quality of life. The common explanation power of the two variables is strong. High disease activity and poor functional status leads to a worse quality of life.

2. Cost-of-illness in PsA

   The average annual cost of PsA is about 1 400 000 HUF/patient.

   Costs of patients with symmetric polyarticular arthritis are the highest. Severity of skin symptoms measured by PASI present the strongest correlation with direct medical costs. Somewhat weaker correlation is detectable between total costs and functional status and disease activity.

Worse skin symptoms, functional status and higher disease activity are associated with higher costs thus our hypothesis was confirmed, more severe disease has higher costs

2.1. Costs of PsA are lower than in RA in all cost domains but the rate of direct and indirect costs are different. Health care utilisation was higher in RA whilst productivity loss due to disability was higher in our PsA sample.

2.2. Review of the literature revealed only one PsA cost-of-illness study from Germany. Costs of PsA are higher in all cost domains compared to Hungary (direct costs 2.1, indirect costs 4.1 times larger). Higher unit costs in Germany explain the difference, leading to higher total costs despite the lower resource utilisation.

We have analysed the health status of the patients with PsA, their therapies and disease related costs of PsA in our research. Data on disease burden are required for health policy decisions. Biological drugs play increasing role in the treatment of PsA improving patients' health status but costs significantly grow as well. Therefore, it is relevant to measure clinical efficacy (on health status, disease progression, quality of life) of new technologies namely biological drugs and analyse their cost-effectiveness. Such data help clinical decisions and are definitely required for value based financing decisions.

Nevertheless, only few international publications are available on cost-of-illness of PsA in Europe. Similarly, PsA related disease burden, costs and cost drivers were not revealed previously in Hungary either.

Our study offers baseline data for further clinical and health economic analysis.

Based on our research, cost-of-illness of PsA in Hungary is notably different from international results. Therefore it is crucial to use country-specific data for cost-effectiveness analysis.

Our results aim to contribute to health policy, financing and clinical decisions in the field of PsA considering specific characteristics of the Hungarian context.

6 List of own publications

6.1 Publications related to the Dissertation

-1- Brodszky V, Péntek M, Gulácsi L. (2008) Efficacy of adalimumab, etanercept and infliximab in psoriatic arthritis based on ACR50 response after 24 weeks treatment. Scand J Rheumatol, 37: 399-400 **IF 2007: 2,640**

-2- Brodszky V, Balint P, Geher P, Hodinka L, Horvath G, Koo E, Pentek M, Polgar A, Sesztak M, Szanto S, Ujfalussy I, Gulacsi L. (2009) Disease Burden of Psoriatic Arthritis Compared to Rheumatoid Arthritis, Hungarian Experiment. Rheum Int, DOI: 10.1007/s00296-009-0936-1 **IF 2007: 1,27**

-3- Koó É, Brodszky V, Péntek M, Ujfalussy I, Nagy MB, Gulácsi L. (2006) A biológiai terápia szerepe az arthritis psoriatica gyógykezelésében. Orv Hetil, 147: 1963-1970.

-4- Brodszky V, Koó É, Péntek M, Ujfalussy I, Gulácsi L. (2009) Comparison of the disease specific PsAQoL and the generic EQ-5D

health related quality of life instruments in PsA; results from a cross-sectional survey. Ann Rheum Dis, 68 Suppl 3: 663.

-5- Brodszky V, Péntek M, Kárpáti K, Boncz I, Sebestyén A, Gulácsi L. (2008) Comparative efficacy of biological treatments in patients with psoriatic arthritis; systematic literature review and meta-analysis. Value Health, 11: A254

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-7- Péntek M, Kobelt G, Czirják L, Szekanecz Z, Poór G, Rojkovich B, Polgár A, Genti G, Kiss CG, Brodszky V, Májer I, Gulácsi L. (2007) Costs of rheumatoid arthritis in Hungary. J Rheumatol, 34: 1437-1439 **IF: 2,940**

6.2 Publications not related to the Dissertation

<u>Original articles in foreign languages</u>

-1- Pentek M, Horvath C, Boncz I, Falusi Z, Toth E, Sebestyen A, Majer I, Brodszky V, Gulacsi L. (2008) Epidemiology of osteoporosis related fractures in Hungary from the nationwide health insurance database, 1999-2003. Osteoporos Int, 19: 243-249 **IF 2007: 3,893**

-2- Brodszky V, Kemeny L, Kárpáti K, Péntek M, Bécsi R, Érsek K, Gulácsi L. Efficacy of biological therapy in the treatment of psoriasis; meta-

analysis of 16 randomized controlled trials. Hungarian Medical Journal, elfogadva

-3- Brodszky V, Péntek M, Kárpáti K, Orlewska E, Gulácsi L. (2008) Analiza ekonomiczna rituksymabu w leczeniu reumatoidalnego zapalenia stawów na Węgrzech (Economic evaluation of rituximab in the treatment of rheumatoid arthritis in Hungary). Farmakoekonomika (Varsó), 12: 10-16.

-4- Brodszky V, Nagy V, Farsang C, Karpati K, Gulacsi L. (2008) The efficacy of indapamide in different cardiovascular outcomes; meta-analysis. Hungarian Medical Journal, 2:181-191.

-5- Brodszky V, Orlewska E, Péntek M, Kárpáti K, Skoupá J, Gulácsi L. Challenges in economic evaluation of new drugs: experience with rituximab in Hungary. Med Sci Monit, **accepted IF 2007: 1,607**

-6- Gulácsi L, Brodszky V, Péntek M, Kárpáti K, Varga S, Vas G, Boncz I. (2009) History of health technology assessment (HTA) in Hungary. Int J Technol Assess Health Care, 25 Suppl 1: 120-126 **IF 2007: 1,406**

<u>Original articles in Hungarian</u>

-1- Kárpáti K, Brodszky V, Májer I, Boncz I, Bereczki D, Gulácsi L. (2007) Az acut stroke előfordulása és betegségterhe hazánkban, OEP adatok alapján. IME, 6: 41-46.

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-3- Brodszky V, Borgström F, Arnetorp S, Péntek M, Gulácsi L. (2009) Az abatacept egészség-gazdaságtani elemzése rheumatoid arthritis kezelésében Magyarországon. Egészségügyi Gazdasági Szemle, 47: 2-9.

-4- Brodszky V, Péntek M, Kárpáti K, Orlewska E, Gulácsi L. (2008) A rituximab kezelés költség-hasznosságának modellezése rheumatoid arthritisben TNF-alfa gátló kezelés után Magyarországon. IME, 7: 41-46.

-5- Brodszky V, Gulácsi L. (2008) Egységesedő technológiaelemzési gyakorlat Európában; az Egészségügyi Technológiaelemzés Európai Hálózata (EUnetHTA). IME, 7: 30-34.

-6- Péntek M, Szekanecz Z, Czirják L, Poór Gy, Rojkovich B, Polgár A, Genti Gy, Kiss Cs, Sándor Zs, Májer I, Brodszky V, Gulácsi L. (2008) Betegségprogresszió hatása az egészségi állapotra, életminőségre és költségekre rheumatoid arthritisben Magyarországon. Orv Hetil, 149: 733-741.

-7- Péntek M, Nagy M, Brodszky V, Tóth E, Géher P, Gulácsi L. (2006) Spondylitis Ankylopoetica-ban szenvedő betegek munkaképessége a szakirodalom szisztematikus áttekintése alapján. Egészségügyi Gazdasági Szemle, 44: 86-93.

-8- Kemény L, Brodszky V, Kárpáti K, Gulácsi L. (2006) A biológiai szerek szerepe a psoriasis gyógykezelésében 9 randomizált, placebokontrollált vizsgálat eredményei alapján. Orv Hetil, 147: 981-992.

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-10- Géher P, Nagy MB, Péntek M, Tóth E, Brodszky V, Gulácsi L. (2006) A biológiai szerek szerepe a spondylitis ankylopoetica gyógykezelésében. Orv Hetil, 147: 1203-1214.

-*11*- Kárpáti K, Brodszky V, Farsang Cs, Jermendy Gy, Vándorfi Gy, Zámolyi K, Gulácsi L. (2006) A carvedilol hatásossága szívelégtelenségben; a nemzetközi szakirodalom szisztematikus áttekintése. Orv Hetil, 147: 1931-1938.

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-15- Brodszky V, Czirják L, Géher P, Hodinka L, Kárpáti K, Péntek M, Poór Gy, Szekanecz Z, Gulácsi L. (2007) A rituximab szerepe a rheumatoid arthritis kezelésében: irodalmi áttekintés. Orv Hetil, 148: 1883-1893.

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