リウマチ科

1．概要

当科は整形外科から発展したが内科的治療を基本とし、外科的治療もおこなっている。当科の診療の４本柱について記す。現在は平野、磯野の２人のリウマチ科常勤医を中心に、研修中の整形外科若手医師の助けも借りて診療にあたっている。

⑴　関節リウマチ（RA）の薬物治療：MTXを中心とした古典的抗リウマチ薬を早期から使用し、効果不十分例には生物学的製剤を導入し関節破壊の防止に努めている。新薬の治験も行っている。

⑵　各種リウマチ性疾患（強直性脊椎炎、乾癬性関節炎、リウマチ性多発筋痛症、SAPHO症候群）：比較的珍しい疾患群であるが対応し、疾患ごとの適切な治療を行っている。

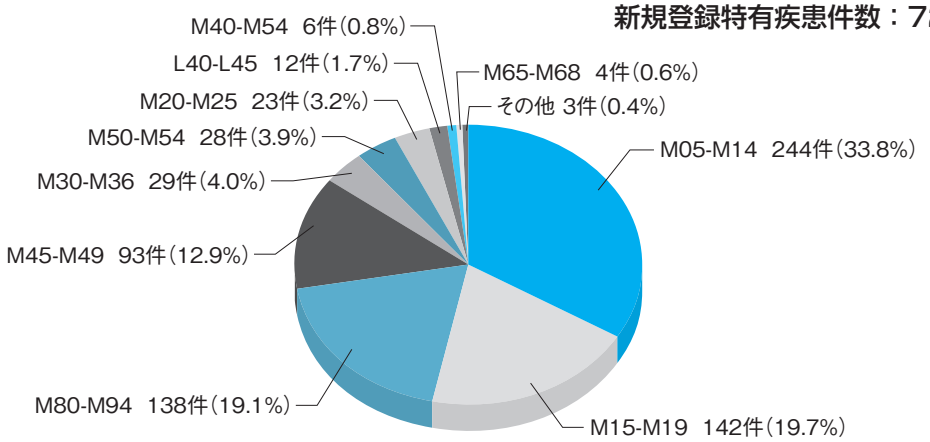
⑶　骨粗鬆症の診療：古典的薬剤に加え、新規薬剤（テリパラチド、デノスマブ）が出現し、パラダイムシフトが起こっている。骨折診療の潮流は治療から予防に向かっている。

⑷　RAの外科的治療：長期罹病RA患者には外科的治療が必要であり、薬物治療とのコンビネーションこそが最高の結果をもたらす。人工関節置換術、関節固定術、関節形成術を行っている。

（部長　平野　裕司）

2．ICD－10による疾患別頻度

新規登録特有疾患件数：722件



ICD-10　中間分類項目
M05-M14：炎症性多発性関節障害
M15-M19：関節症
M80-M94：骨障害及び軟骨障害
M45-M49：脊椎障害
M30-M36：全身性結合組織障害
M50-M54：その他の脊柱障害
M20-M25：その他の関節障害
L40-L45：丘疹落せつ<屑><りんせつ<鱗屑>>性障害
M40-M54：脊柱障害
M65-M68：滑膜及び腱の障害

3．活動報告

(1) 実績

2015年度関節リウマチ患者背景		
症例数(件)		930
新患者数(各年)(人)		60
性別	男(人)	224
	女(人)	706
	女性率(%)	75.9
平均年齢(歳)		65.3
平均罹病期間(年)		13.6
罹病期間分類(%)	2年以下	15.6
	3年～9年	30.4
	10年以上	54.0
Stage(%)	Ⅰ	22.7
	Ⅱ	16.5
	Ⅲ	22.7
	Ⅳ	38.1
Class(%)	1	35.7
	2	47.9
	3	13.2
	4	3.2
RF陽性率(%)		76.7
ACPA陽性率(%)		81.6

2015年度関節リウマチ薬物治療	
MTX投与者	601
MTX投与率(%)	64.6
投与例の平均MTX投与量(mg/w)	8.7
アザルフィジン投与者	187
アザルフィジン投与率(%)	20.1
プログラフ投与者	163
プログラフ投与率(%)	17.5
PSL投与率(%)	21.5
投与例の平均PSL投与量(mg/day)	3.9
生物学的製剤経験者	309
生物学的製剤経験率(%)	33.3

2015年度関節リウマチ臨床成績		
平均CRP（mg/dl）		0.69
平均DAS28（ESR）		2.93
DAS28（ESR）疾患活動性分類（%）	High	5.5
	Moderate	30.1
	Low	19.0
	Remission	45.5
平均SDAI		7.0
SDAI疾患活動性分類（%）	High	2.7
	Moderate	16.3
	Low	42.6
	Remission	38.4
Boolean4（%）		31.0
平均mHAQ		0.427
mHAQ<0.5（%）		66.8

2015年リウマチ科手術	
合計手術件数	26
人工膝関節置換術	9
人工股関節置換術	5
足趾形成術	5
RA手関節手術	1
足関節固定術	1
人工膝関節片顆置換術	1

学会発表（医局）

＜リウマチ科＞

No.	演　題　名	区分	氏名	学会・研究会名	発表年月日
1	多施設研究所（TBCR-plus）による関節リウマチにおけるイグラチモドの52週治療成績の解析－投与開始時の疾患活動性の影響－	筆頭演者	平野　裕司	第59回日本リウマチ学会総会・学術集会	2015/4/23
2	関節リウマチにおけるMTX週16㎎投与の有効性と安全性の解析	筆頭演者	平野　裕司	第59回日本リウマチ学会総会・学術集会	2015/4/23
3	関節リウマチにおける継続率から見た生物学的製剤治療の長期予後の検討	筆頭演者	平野　裕司	第59回日本リウマチ学会総会・学術集会	2015/4/23
4	関節リウマチにおけるゴリムマブの有効性予測因子～多施設研究データより～	筆頭演者	平野　裕司	第59回日本リウマチ学会総会・学術集会	2015/4/23
5	トシリズマブが中止となった関節リウマチ患者におけるTNF阻害薬とアバタセプトの臨床効果の比較－多施設研究TBCRよりー	筆頭演者	平原　慎也	第59回日本リウマチ学会総会・学術集会	2015/4/23
6	関節リウマチにおける2年間のトシリズマブ治療が、疾患活動性、生活の質、関節破壊防止に与える影響～MTXとPSLの減量に注目 して～	筆頭演者	平野　裕司	第59回日本リウマチ学会総会・学術集会	2015/4/23
7	関節リウマチにおいて耐糖能異常は生物学的製剤治療の長期継続率を低下させる	筆頭演者	磯野　正晶	第59回日本リウマチ学会総会・学術集会	2015/4/24
8	肺合併症を有する関節リウマチ患者に対するabataceptの安全性と治療効果の検討－多施設共同研究TBCRよりー	筆頭演者	平原　慎也	第59回日本リウマチ学会総会・学術集会	2015/4/24
9	関節リウマチの骨粗鬆症に対するデノスマブの早期効果－多施設研究TBCR-BONEよりー	筆頭演者	平野　裕司	第59回日本リウマチ学会総会・学術集会	2015/4/25
10	関節リウマチの骨粗鬆症に対するテリパラチド連日投与製剤２年投与の効果～経口プレドニゾロン併用の影響～	筆頭演者	平野　裕司	第59回日本リウマチ学会総会・学術集会	2015/4/25
11	関節リウマチ患者における潜在的結核感染スクリーニングとしてのT-SPOTとクオンティフェロン 2G、3G の比較検討	筆頭演者	平原　慎也	第59回日本リウマチ学会総会・学術集会	2015/4/25
12	関節リウマチ患者の疾患関連因子がロコモティブ症候群発症に与える影響	筆頭演者	平野　裕司	第27回日本リウマチ学会中部支部学術集会	2015/9/4
13	関節リウマチに対するトシリズマブ皮下注製剤の使用経験	筆頭演者	平原　慎也	第27回日本リウマチ学会中部支部学術集会	2015/9/4
14	トシリズマブ治療中に高ビリルビン血症を呈した関節リウマチの３症例	筆頭演者	平野　裕司	第27回日本リウマチ学会中部支部学術集会	2015/9/4
15	関節リウマチの骨粗鬆症でのテリパラチド連日製剤の後療法のミノドロネート+エルデカルシトールとデノスマブの比較	筆頭演者	平野　裕司	第27回日本リウマチ学会中部支部学術集会	2015/9/5
16	インフリキシマブを使用した乾癬性関節炎の２例	筆頭演者	福井　　順	第27回日本リウマチ学会中部支部学術集会	2015/9/6
17	関節リウマチの骨粗鬆症に対する2年間のテリパラチド連日投与製剤の効果に対する併用薬剤（経口プレドニゾロンと生物学的製剤）の影響	筆頭演者	平野　裕司	第17回日本骨粗鬆症学会	2015/9/17

学会発表（医局）

＜リウマチ科＞

No.	演　　題　　名	区分	氏名	学会・研究会名	発表年月日
18	関節リウマチの骨粗鬆症でのテリパラチド連日製剤の後療法のミノドロネート+エルデカルシトールとデノスマブの比較検討	筆頭演者	平野　裕司	第17回日本骨粗鬆症学会	2015/9/17
19	関節リウマチの骨粗鬆症に対するデノスマブの短期臨床成績－TBCR-BONEより－	筆頭演者	平野　裕司	第17回日本骨粗鬆症学会	2015/9/17
20	当院におけるテリパラチド週一回投与製剤の使用経験	筆頭演者	磯野　正晶	第17回日本骨粗鬆症学会	2015/9/17
21	関節リウマチの骨粗鬆症に対するエルデカルシトールの臨床成績－第２報－	筆頭演者	平野　裕司	第17回日本骨粗鬆症学会	2015/9/19
22	TNFに対する抗体製剤の共通点と相違点－インフリキシマブ、アダリムマブ、ゴリムマブ－	筆頭演者	平野　裕司	第43回日本関節病学会	2015/11/5
23	関節リウマチの骨粗鬆症に対するデノスマブの有効性予測要因～12か月経過例での検討～	筆頭演者	平野　裕司	第43回日本関節病学会	2015/11/5
24	関節リウマチにおける２年間のアバタセプト治療の成績～併用薬剤の減量に注目して～	筆頭演者	平野　裕司	第43回日本関節病学会	2015/11/6
25	関節リウマチの骨粗鬆症におけるデノスマブの治療成績	筆頭演者	福井　　順	第30回日本臨床リウマチ学会	2015/11/21
26	関節リウマチの骨粗鬆症におけるテリパラチド連日投与製剤の後療法のミノドロネート+エルデカルシトールとデノスマブの比較	筆頭演者	平野　裕司	第30回日本臨床リウマチ学会	2015/11/21
27	関節リウマチに対するトシリズマブ皮下注製剤の使用経験	筆頭演者	平原　慎也	第30回日本臨床リウマチ学会	2015/11/21

研究会発表（医局）

＜リウマチ科＞

No.	演　題　名	区分	氏名	学会・研究会名	発表年月日
1	当院におけるWeekly PTH製剤の使用経験	筆頭演者	磯野　正昌	第３回全三河リウマチ研究会	2015/3/14
2	関節リウマチ患者における潜在的結核感染スクリーニングとしてのT-SPOTとクオンティフェロン2G、3Gの比較検討	筆頭演者	平原　慎也	第３回全三河リウマチ研究会	2015/3/14
3	関節リウマチの骨粗鬆症に対するエルデカルシトールの長期臨床成績～２年継続例について～	筆頭演者	平野　裕司	第３回三河骨粗鬆症研究会	2015/3/21
4	関節リウマチにおけるゴリムマブの有効性予測因子～多施設研究データより～	筆頭演者	平野　裕司	第42回東三河リウマチ研究会	2015/5/16
5	関節リウマチにおけるMTX週16㎎投与の有効性と安全性の解析	筆頭演者	平野　裕司	第36回リウマチセンター間連絡会	2015/7/11
6	関節リウマチにおけるMTX週16㎎投与の有効性と安全性の解析	筆頭演者	平野　裕司	第３回愛知DMARDs研究会	2015/10/3
7	関節リウマチの骨粗鬆症に対するデノスマブの有効性予測因子～12ヶ月経過例での検討～	筆頭演者	平野　裕司	第４回三河骨粗鬆症研究会	2015/10/17

講　　演（医局）

＜リウマチ科＞

No.	演　　題　　名	演者名	学会・研究会名	発表年月日
1	整形外科リウマチ専門医が考える関節リウマチ診療における治療タイミング	平野　裕司	第96回岐阜県整形外科集団会	2015/1/31
2	骨粗鬆症治療におけるデノスマブの可能性	平野　裕司	豊橋骨粗鬆症治療研究会	2015/2/14
3	米国リウマチ学会からの最新情報とシンポニー有効性の予測因子について	平野　裕司	RA病診連携セミナー	2015/2/19
4	生物学的製剤治療における、MTXの最適な使用方法について	平野　裕司	EFFORT Consortium 2015	2015/2/21
5	抗TNF製剤の臨床的パフォーマンス	平野　裕司	高知県整形外科医会学術講演会	2015/2/26
6	整形外科リウマチ専門医が考える関節リウマチを中心としたRheumatology	平野　裕司	第３回全三河リウマチ研究会	2015/3/14
7	リウマチ患者さんに知っておいて欲しい事～安心で快適な生活をするために～	平原　慎也	第53回豊橋市民病院リウマチ講演会	2015/3/20
8	ゴリムマブのPerformanceとPrediction	平野　裕司	Golimumab Expert Seminar	2015/4/11
9	生物学的製剤治療におけるMTXの最適な使用法について	平野　裕司	東北BIOリスクマネジメント研究会～生物学的製剤を安全に使っていくために～	2015/5/9
10	整形外科リウマチ専門医が考える関節リウマチを中心としたRheumatology	平野　裕司	2015年岡山リウマチコラボ・セミナー	2015/5/21
11	臨床データから考えるトシリズマブ有効利用マニュアル	平野　裕司	静岡IL-6研究会	2015/5/29
12	当科におけるトファチシニブ使用経験	平野　裕司	ゼルヤンツカレッジ in Tokyo-How to use in clinical site-	2015/5/30
13	関節リウマチと診断してメトトレキサートを処方するまでの簡易マニュアル	平野　裕司	リウマチ学の門をたたく会～リウマチのは良くなる病気です～	2015/6/6
14	関節リウマチ診療における看護師の役割	平野　裕司	看護師のための関節リウマチセミナー	2015/6/17
15	現代のリウマチ治療の課題について	平野　裕司	第７回中村・中川関節リウマチ研究会	2015/6/18
16	骨粗鬆症診療　Update	平野　裕司	生涯教育研修会	2015/6/19
17	関節リウマチにおけるイグラチモドの有用性－全例調査中間報告と多施設研究データの紹介－	平野　裕司	DMARDsを語る会in東海	2015/6/20
18	関節リウマチの重要な合併症－骨粗鬆症について－	平野　裕司	第12回市民公開講座	2015/6/21
19	関節リウマチにおける２年間のアバタセプト治療の成績/関節リウマチにおけるロコモティブ症候群	平野　裕司	ESCORT East mikawa Abatacept for Rheumatoid Treatment Seminar	2015/6/26
20	関節リウマチの診断～関節エコーの役割を含めて～	平野　裕司	岐阜RA　Young　Academy	2015/7/3
21	関節リウマチの骨粗鬆症にフォルテオを使用する際のClinical Questions	平野　裕司	FORTEO National Web Conference	2015/7/16
22	整形外科リウマチ専門医が考える関節リウマチを中心としたRheumatology	平野　裕司	第27回長野リウマチ勉強会講演会	2015/7/18
23	健康日本21の中心課題としてのロコモティブシンドローム	平野　裕司	濱松一中・浜松北高同窓会総会	2015/7/25
24	整形外科リウマチ専門医が考える関節リウマチを中心としたRheumatology	平野　裕司	豊橋市薬剤師会研修会	2015/8/20
25	ゴリムマブのPerformanceとPrediction	平野　裕司	RA Best Treatment Meeting in HYOGO	2015/9/26

講　　演（医局）

＜リウマチ科＞

No.	演　　題　　名	演者名	学会・研究会名	発表年月日
26	抗TNF製剤の臨床的パフォーマンス	平野　裕司	第4回川口関節の治療を考える会	2015/10/23
27	骨粗鬆症や肺障害などの合併症を考慮した現代の関節リウマチ治療	平野　裕司	第６回旭川Tcellセミナー	2015/10/29
28	関節リウマチにおけるゴリムマブのPerformanceとPrediction	平野　裕司	第43回日本関節病学会ランチョンセミナー１	2015/11/5
29	多施設研究の臨床データから考える関節リウマチ薬物治療におけるMTXとアダリムマブの効果的な使用法	平野　裕司	第130回西日本整形外科・災害外科学会ランチョンセミナー	2015/11/14
30	骨粗鬆症の予防と治療のガイドライン2015年版のポイントとSERMの役割	平野　裕司	女性のミカタフォーラム	2015/11/17
31	実臨床から考えるメトトレキサートとトシリズマブの併用療法のベストユース	平野　裕司	第30回日本臨床リウマチ学会イブニングセミナー３	2015/11/21
32	臨床データから考えるトシリズマブ有効利用マニュアル	平野　裕司	岐阜IL-6阻害療法研究会2015	2015/11/26
33	臨床データから考えるトシリズマブ有効利用マニュアル	平野　裕司	東濃リウマチ薬物治療研究会	2015/12/3
34	関節リウマチ診療の最新の動向	平野　裕司	愛知県病院薬剤師会学術講演会	2015/12/8
35	関節リウマチ診療の最新の動向	平野　裕司	薬剤師のためのリウマチセミナー	2015/12/10

Ⅵ　研究・業績

【国際学会】

(1) リウマチ科　医員　磯野　正晶

Annual European Congress of Rheumatology (EULAR 2015) in Rome

INFLUENCE OF DIABETES MELLITUS ON DRUG SURVIVAL AND TREATMENT EFFICACY OF BIOLOGICS THERAPY IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Biologics (BIO) therapy has become general treatment in rheumatoid arthritis (RA) patients. One goal of BIO therapy is to stop BIO therapy after reaching targets to treat (Bio-free), another goal is to continue BIO therapy and sustain targets to treat. Some patients drop out from the BIO therapy for several reasons. In previous study, we found patient with diabetes mellitus (DM) might have low drug survival on BIO therapy.

Objectives: The purpose of this retrospecitv study was to investigate the investigate the influence of DM on drug survival and treatment efficacy of BIO therapy in RA patients.

Methods: A retrospective single-center study was conducted in patients with RA who started any of BIO (infliximab, etanercept, adalimumab, tocilizumab, abatacept, golimumab) between 2003 and 2013 in our institute. Patients were divided into two groups: diabetics (group D) and non-diabetics (group N). Baseline characteristics, BIO therapy continuation rate, and reasons for discontinuation were analyzed and compared with two groups using Chi squared test, Mann–Whitney U test, Wilcoxon signed-rank test and log-rank test. Switching one BIO to another was defined as continuation of BIO therapy. Treatment efficacy and quality of life (QOL) were assessed and compared in both groups at baseline and the last observation day, using the DAS28-CRP, SDAI, and the modified health assessment questionnaire (mHAQ).

Results: A total of 245 patients were studied (30 patients for group D / 215 patients for group N). RA duration, methotrexate (MTX) dose, prednisolone (PSL) dose, DAS28-CRP, SDAI, and mHAQ were similar between two groups at baseline (13.5±14.0 years vs. 10.8±10.3 years, 9.4±2.6 mg/week vs. 8.5±2.6 mg/week, 5.1±1.4mg/day vs. 5.0±1.5 mg/day, 5.0±0.97 vs. 4.7±1.2, 27.9±11.1 vs. 25.4±13.0, 1.0±0.7 vs. 0.8±0.7, for group D and group N, respectively; p>0.05 for all). We found significant difference between group D and group N at baseline in mean age (65.4±6.8 vs. 56.7±13.1 p<0.01), %female (63.3% vs. 85.5% p=0.03), RF positive rate (93.3% vs. 77.2% p=0.04), estimated glomerular filtration rate (77.6 ml/min/1.73 m2 vs. 92.9 ml/min/1.73 m2p<0.01), PSL-concomitant rate (83.3% vs. 52.5% p<0.01), and MTX-concomitant rate (60.0% vs. 85.6%p<0.01). Drug survival of BIO therapy was significantly shorter in group D than in group N (Fig. 1).Continuation rate after 1, 3, 5 years was 76.4%, 68.9%, 41.3% for group D, and 90.5%, 83.6%, 75.2% for group N (p<0.01). The most common reason for quitting BIO therapy was infection in both groups. The rate of infection leading to discontinuation of BIO therapy was significantly higher in group D than in group N (16.7% vs. 5.6% p=0.03). Treatment efficacy and QOL at the last observation were significantly worse in group D than in group N (DAS28-CRP 3.07±1.49 vs. 2.05±0.97, SDAI 12.7±12.7 vs. 5.64±6.23 and

mHAQ 0.69 ± 0.52 vs.0.46 ± 0.59, for group D and group N, respectively; $p<0.01$ for all).

Conclusions: Our data suggest that diabetic RA patients have high risk of infection leading to discontinuation of BIO therapy. The short drug survival of BIO therapy may be the reason for the poor treatment efficacy at the last observation in diabetic RA patients compared with that of non-diabetic RA patients. We conclude that DM is one of the considerable factors when starting the BIO therapy in RA patients.

(2) リウマチ科　部長　平野　裕司

Annual European Congress of Rheumatology (EULAR 2015) in Rome

ANALYSIS OF TREATMENT RETENTION RATE OF BIOLOGICS THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS - A SINGLE CENTER COHORT STUDY -

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Background: Biologics (Bio) therapy has become a standard therapy in the treatment of rheumatoid arthritis (RA) and long-term outcomes can be evaluated recently. Although one of the desirable treatment strategy is to stop Bio therapy after reaching targets to treat such as remission or low disease activity (Bio-free), other desirable treatment strategy is to continue Bio therapy and to sustain targets to treat. Several studies showed it difficult to continue Bio-free for a long time, so it is a practical strategy to continue Bio therapy in clinical setting.

Objectives: This observational cohort study investigated the treatment retention rate of Bio therapy and the predictors of its continuation in patients with RA.

Methods: 254 RA patients who initiated any of biologic agents (infliximab, etanercept, adalimumab, tocilizumab, abatacept, golimumab) as first Bio in our institute from 2003 to 2013 were included in this study. Switching from one Bio agent to another was defined as continuation of Bio therapy in this study. Patients' characteristics and treatment retention rate were investigated. The outcomes at last observation in both the Bio-continued and the Bio-stopped were compared with each other. Bio-free due to remission and stopping Bio therapy related to pregnancy were assigned to the Bio-continued. The predictors for continuation of the Bio therapy were also investigated.

Results: Baseline characteristics was as follows. % female was 82.7%. Mean age was 57.8 years old. Mean RA duration was 11.3 years. % methotrexate (MTX) concomitant was 81.5% and mean used dose was 8.5mg/weeks (MTX dose was restricted up to 8mg/weeks until 2011 in Japan and 16mg/w after 2011). %prednisolone (PSL) concomitant was 56.3%. % Bio monotherapy was 13.6%. Mean baseline DAS28-CRP and SDAI was 4.74 and 25.8, respectively. % high disease activity measured using DAS28 and SDAI at baseline was 41.7% and 46.3%, respectively. Baseline disease activity were getting lower year by year. Treatment continuation rates using Kaplan-Meier method were 88.4% at 1 year, 82.1% at 3 years, 74.4% at 5 years and 70.4% at 7 years. Reasons for stopping Bio therapy were infection at first, hope of patients or absent to hospital at second and worsened comorbidities at third. Lower disease activity and more remission rates were observed in the Bio- continued compared with the Bio-stopped. Predictors of continuation of Bio therapy were shorter RA duration, fewer concomitant prednisolone, more concomitant MTX, lower disease activity, good renal function, fewer lung disease and glucose intolerance in univariate analysis. Concomitant MTX, heavy body weight and glucose tolerance (defined as patients with abnormal HbA1c or treated with drugs for diabetes mellitus) was detected as predictors of continuation of Bio therapy in multivariate analysis.

Conclusions: Our cohort study showed that long-term continuation rate of Bio therapy was about 60-70% in 7-8 years. Infection was the most reasons for stopping Bio therapy. Baseline characteristics of RA patients who initiated Bio therapy were one of the important predictors for continuation of Bio. Comorbidities were one of the important influencers on treatment retention rate of Bio therapy and glucose intolerance was the most important influencer in this study.

(3) リウマチ科　部長　平野　裕司

Annual European Congress of Rheumatology (EULAR 2015) in Rome

PREDICTORS OF EFFECTIVENESS IN GOLIMUMAB TREATMENT AND EFFICACY OF DOSEESCALATION OF GOLIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS -A MULTICENTER REGISTRY STUDY TBCRY.

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Background: Golimumab (GLM) is a human anti-tumor necrosis factor (TNF) alpha monoclonal antibody and shown to be effective in the treatment of rheumatoid arthritis (RA). Although early prediction of the efficacy of GLM is important for early modification of treatment, the information is lacking. Although one of the modifications in the GLM treatment is dose-escalation of GLM from 50mg to 100mg every 4 week, the information of dose-escalation is also lacking in the clinical setting.

Objectives: This retrospective observational study investigated (1) the efficacy and the drug retention rate of GLM in Japanese clinical setting, (2) the predictors of efficacy of GLM treatment and (3) the efficacy of doseescalation of GLM due to lack of efficacy using the multicenter registry data in Japan (Tsurumai Biologics Communication registry: TBCR).

Methods: 111 RA patients treated with GLM were used in this study. Patients' characteristics, time course of disease activity and drug retention rate using Kaplan-Meier method were investigated. Good outcome group (GOgroup: DAS28-CRP<2.6 at 52 weeks) and not-good outcome group (NGOgroup) were compared with each other with respect to baseline characteristics, baseline disease activity and disease activity at 4 weeks. The dose-escalation cases (n=14) were compared with the cases treated with GLM 50mg (n=25) with respect to patients' characteristics and the efficacy of dose-escalation was also evaluated.

Results: 93 female and 18 male were included. Mean age was 61.9 years old. Mean RA duration was 158.4 months. MTX usage was 73.0%. PSL usage was 54.3%. Bio-naive was 53.2%. Mean DAS28-CRP and mean SDAI at 0w-4w-12w-24w-52w were 3.99-3.24-2.92-2.81-2.72 and 20.6-14.0-11.0-10.2-9.5, respectively. Both DAS28-CRP and SDAI were significantly decreased after 4 week. Drug retention rate of GLM was 79.2% at 1 year and 77.1% at 2 year. Reasons for stopping GLM were lack of efficacy in 6 cases, adverse event in 5 cases and others in 4 cases. Age, MMP-3 at 0w, TJC at 4w, ESR at 4w, MMP-3 at 4w, DAS28-CRP at 4w and SDAI at 4w in GOgroup were significantly low compared with those in NGOgroup. AUC of MMP-3 at 0w, TJC at 4w and DAS28-CRP at 4w were over 0.7 using ROC analysis and cut-off values were 133.3ng/ml,3 and 3.09, respectively. MMP-3 at

initiation of GLM treatment in the dose-escalation cases was significantly high compared with that in GLM50mg cases (253.5 vs. 9.8, p=0.043). Cut-off value of MMP-3 at 0w for prediction of dose-escalation was 99.7ng/ml using ROC analysis (AUC=0.714). DAS28-CRP and CRP were improved after dose escalation of GLM in dose-escalation cases.

Conclusions: GLM was effective in RA patients in Japanese clinical setting. Effectiveness at 52w could be predicted using baseline characteristics and early response in GLM treatment. Serum MMP-3 was one of the predictors for effectiveness at 52w and dose-escalation. In conclusion, RA patients with high MMP-3 and RA patients without good early response at 4 week may be necessary to be treated with GLM 100mg in the early time of GLM treatment.

⑷ リウマチ科　部長　平野　裕司

Annual European Congress of Rheumatology (EULAR 2015) in Rome

DAILY TERIPARATIDE TREATMENT FOR TWO YEARS ON OSTEOPOROSIS IN PATIENTS WITH RHEUMATOID ARTHRISIS－IMPACT OF CONCOMITANT DRUGS(PREDNISOLONE AND BIOLOGICS)ON EFFECTS OF TERIRARATIDE -

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Background: Although medication of rheumatoid arthritis (RA) has been improved by early intensive treatment using MTX and biological agents (BIO) for decades, treatment of concomitant disease in RA patients, such as osteoporosis (OP), will be more important to improve activity of daily living of RA patients.
We reported two-year outcome of daily teriparatide (TPTD) on OP in RA patients in EULAR 2014. TPTD has a strong effect on bone metabolism and increases bone mineral density (BMD). Although prednisolone (PSL) and BIO that are often used in RA patients also have strong effects on bone metabolism, the interaction between TPTD and these drugs have not well-understood.

Objectives: This prospective study investigated the impacts of PSL and BIO on the efficacy of TPTD on OP in RA patients.

Methods: 50 females with both OP and RA were included in this study. 2 years had passed after initiation of TPTD. At first, all patients were divided into two groups, which were PSL-concomitant (PG) and Non-PSL-concomitant (NPG). Patients' characteristics, BMD in lumbar spine (LS) and total hip (TH) and change of bone turnover markers (BTMs: BAP, P1NP, NTX, TRACP-5b) were compared between two groups. Next, all patients were divided into two groups, which were BIO-concomitant (BG) and Non-BIO-concomitant (NBG).
Change of BMD and BTMs were also compared between two groups.

Results: [Baseline patients' characteristics] Mean age was 71.0 years old. Mean RA duration was 19 years.
Mean DAS28-CRP and mHAQ were 2.73 and 1.147, respectively. Mean FRAX was 37.4%. [PG (n=35) vs. NPG (n=15)] RA duration in PG was significantly long compared with that in NPG. mHAQ in PG was significantly high compared with that in NPG. Although LS-BMD and TH-BMD in both groups has significantly increased after initiation of TPTD, %increase of BMD in PG tended to be lower than that in NG and there was a significant difference in %increase of TH-BMD at 6 months between in PG and in NPG (-0.5% vs. 3.3%). Dose dependency of PSL in TH-BMD was found.

Although BTMs in PG tended to be lower than that in NPG, the differences were not significant. [BG (n=18) vs. NBG (n=32)] Although LS-BMD in BG and NBG and TH-BMD in NBG have significantly increased after the initiation of TPTD, TH-BMD in BG has not. %increases in LS-BMD in BG at 6 months and 18 months were significantly low compared with that in NBG. %increase in TH-BMD in BG at 24 months was significantly low compared with that in NBG. In contrast, % increase of four BTMs in BG was significantly high compared with that in NBG.

Conclusions: This study suggested both PSL and BIO modified the effects of TPTD on bone metabolism. %increase of BMD in RA patients taking PSL tended to be low. So, oral PSL should be tapered during TPTD treatment. It was suggested that BIO use decreased the effect of TPTD with respect to %increase in BMD. In contrast, % increase of BTMs in BG was high compared with that in NBG. This is, what is called, the paradoxical response between increase of BMD and BTMs in RA patients treated both BIO and TPTD.

References: 1) Y. Hirano et al. EFFICACY OF DAILY TERIPARATIDE FOR TWO YEARS ON OSTEOPOROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS-IS IT APPROPREATE TO COMBINE DAILY TERIPARATIDE AND BIOLOGICAL AGENTS?˜. Ann Rheum Dis 2014; 73(Suppl2)

⑸ リウマチ科　部長　平野　裕司

American Society of Bone and Mineral Research 2015 (ASBMR 2015) in Seattle

Comparative Study between Denosumab and Minodronate with Eldecalcitol as the Treatment after 2-Year Daily Teriparatide in Osteoporosis in Patients with Rheumatoid Arthritis

Abstract

Comparative Study between Denosumab and Minodronate with Eldecalcitol as the Treatment after 2-Year Daily Teriparatide in Osteoporosis in Patients with Rheumatoid Arthritis

Author(s)

Yuji Hirano, Shinya Hirabara, Masaaki Isono

Background: Although daily teriparatide (dTPTD) treatment greatly increases bone mineral density(BND),increase of BND is not enough after 2-year dTPTD treatment in some patients with osteoporosis(OP). It is Known that no treatment after dTPTD treatment results in decrease of BMD. Although effective treatment strategy after 2-year dTPTD treatment is necessary, it is controversial This Prospective study compared minodronate with eldecalcitol (MIN/ELD) and denosumab (DMB) as the treatment after 2-year dTPTD treatment in OP in patients with rheumatoid arthritis (RA-OP).

Methods: Female RA-OP patients treated with MIN/ELD (n=21) or DMB(n=10) after dTPTD were used. Patients' characteristics, change of BMD (lumber spine and total hip: LSBMD and THBMD) measured by DEXA at every 6 month from the initiation of dTPTD and change of bone turnover markers (BTM) (P1NP and TRACP-5b) at every 6 month from the initiation of dTPTD were compared between two group. DMB (60mg) was injected every 6month with prescribing of native vitamin D and calcium. MIN (50mg) was administered every 4 weeks and ELD (0.75μg) was administered every day. MIN is a bisphosphonate drug and ELD is activated vitamin D.

Results: Patients' characteristics (MIN/ELD: DMB) : Mean age (70.2:70.8). Body mass index (20.8: 21.3). FRAX (39.6%: 33.8%). PSL use (71.4%: 70.0%). No significant differences in patients' characteristics were observed between two groups, %increase of LSBMD (dTPTD 6m/12m/18m/24m/AfterTPTD6m): 7.0/11.7/12.3/12.0/16.8 in MIN/ELD and 10.3/13.7/15.2/16/1/18.4 in DMB. % increase of LSBMD after dTPTD treatment was 4.4% in MIN/ELD and 1.8% in DMB, respectivery. No significant differences were observed at all time-points. % increase of THBMD: 1.2/3.1/4.3/5.9 in MIN/ELD and 1.5/4.4/4.7/4.7/6.5 in DMB. % increase of THBMD after dTPTD treatment was 0.6% in MIN/ELD and 1.1% in DMB, respectively.NO significant difference were observed at all time-points. % change of BTM was expressed as the value at the initiation of dTPTD was 100. P1NP:100/413.9/355.7/258.5/219.2/44.5 in MIN/ELD. 100/407.4/380.5/272.8/228.6/56.9 in DMB.

TRACP: 100/14/.9/157.4/139.8/144.7/51.2 in MIN/ELD. 100/188.0/209.7/178.5/178.6/91.9 in DMB. There were no significant differences in BTM between two groups.

Conclusions: This study shows that short-term efficacy of MIN/ELD equals to that of DMB as the treatment option after –year TPTD in RA-OP. Long-term results are necessary in the future.

⑹ リウマチ科　部長　平野　裕司

American Society of Bone and Mineral Research 2015 (ASBMR 2015) in Seattle

The Short-Term Efficacy of Denosumab in Osteoporosis in Patients with Rheumatoid Arthritis from a Japanese Multicenter Registry

Abstract

The Short – Term Efficacy of Denosumab in Osteoporosis in Patients with Rheumatoid Arthritis from a Japanese Multicenter Registry

Author(s)

Yuji Hirano, Yasuhide Kanayama, Shinya Hirabara, Syuji Asai, Nobunori Takahashi, Takayasu Ito, Naoki Ishiguro, Toshihisa Kojima

Purpose: Osteoporosis (OP) is one of the important comorbidities in rheumatoid arthritis (RA). Pathogenesis of RA-OP is composed from multiple factors, such as hyper cytokine, concomitant drugs and disuse. Although denosumab (DMB), a fully – human anti-RANKL antibody, is expected to be a good treatment for RA-OP, clinical data form real-world is limited. This study investigated the effects of DMB on RA-OP from a multicenter registry data in Japan (TBCR-BONE).

Methods: 53 RA-OP cases were includet. (1) %increase of bone mineral density (BMD) in lumbar spine (LSBMD) and total hip (THBMD) at 6month, (2)%change of bone turnover markers(P1NP and TRACP-5b)at 6m,(3)correlation between change of BMD and change of BTM,(4)results until 12m(n =16), (5) the influence of concomitant use of biological agents (BIO) for the treatment of RA and (6) adverse events were investigated.

Results: Patients' characteristics: 50 females and 3 malts. Mean age: 69.7 years old. RA duration: 14.2 years. Mean body mass index: 19.8. FRAX: 27.1%. Prednisolone use: 45.3% (mean doses: 4.3mg/day). BIO for the treatment of RA was concomitant in 34.0%.

Treatment naive of OP was 35.8%. Cases after teriparatide (TPTD) treatment ware 11 cases. (1) LSBMD (g/cm2) was significantly increased from 0.825 at baseline to 0.857 at 6m (mean %increase:3.9%). THBMD (g/cm2) was significantly increased from 0.598 at baseline to 0.611 at 6m (3.1%). (2) Both P1NP and TRACP-5b were significantly decreased at 6m (41.4% and 34.8% decrease, respectively). (3) There were no significant correlation between % change of BMD at 6m and % change of BMD at 6m and %change of BTM at 6m. (4)%increase of LSBMD was 5.1% at 6m and 6.3% at 12m. %increase of THBMD was 2.4% at 6m and 5.6% at 12m. BTMs were decreased at 6m and unchanged at 12m. (5)Baseline THBMD of BIO group was significantly low compared with that of NonBIO group. TRACP-5b of BIO group was significantly high compared with that of NonBIO group. %increase of LSBMD at 6m was 4.7% in BIO group and 3.0% in NonBIO group. %increase of THBMD at 6m was 3.4% in BIO group and 3.0% in NomBIO group. No significant differences were observed. (6) Hypocalcemia was occurred in 2 and pelvis fracture was occurred in one. Pelvis fracture was healed.

Conclusions: The short-term results of DMB of DMB of RA-OP was good especially in THBMD. This study showed that %change of BTMs were not the predictor for efficacy of DMB on BMD increase at 6m. BIO did not affect the efficacy of DMB.

(7) リウマチ科　副部長　平原　慎也

Annual European Congress of Rheumatology (EULAR 2015) in Rome

THE SAFETY AND TREATMENT EFFICACY OF ABATACEPT IN RHEUMATOID ARTHRITIS PATIENTS WITH INTERSTITIAL LUNG DISEASE: FROM THE TSURUMAI BIOLOGICS COMMUNICATION REGISTRY (TBCR) MULTICENTER STUDY

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Background: Roughly 10-30% of rheumatoid arthritis (RA) patients reportedly develop pulmonary complications. These patients are at increased risk of MTX or biologics-induced damage, which often becomes problematic for RA treatment. Abatacept (ABT) has been reported to have relatively few adverse events, and is often used in clinical settings in patients with pulmonary complications. Given the paucity of studies on the safety of ABT, however, accumulation of safety data under actual clinical settings is warranted.

Objectives: In the present study, we examined the persistence rates and treatment effects of ABT in patients with interstitial lung disease.

Methods: We divided 365 RA patients registered in the Tsurumai Biologics Communication Registry who used ABT for ≥52 weeks according to whether they had interstitial lung disease (ILD group: n=48) or not (N group: n=317). We then compared the continuation rates, incidence of adverse events, and disease activity between the two groups.

Results: No significant differences were found between groups with regard to mean age (ILD group, 66.7 ± 8.6; N group, 64.6 ± 12.4), disease duration (ILD group, 11.5 ± 9.2; N group, 11.9 ± 13.8), or concomitant dose of MTX (ILD group, 7.8mg/week; N group, 7.5mg/week) at the time ABT was initiated, but significant differences were found in the percentage of women (ILD group, 65.9%; N group, 81.4%), concomitant use rates of MTX (ILD group, 21.3%; N group, 52.9%), concomitant use rates of steroid (ILD group, 65.2%; N group, 51.8%), CRP (ILD group, 2.8 ± 3.1; N group, 2.0 ± 2.5), or DAS28-CRP (ILD group, 4.7 ± 1.3; N group, 4.3 ± 1.3). The continuation rates for 52 weeks were 79.2% and 80.8% in the ILD and N groups, respectively (Figure 1a). Adverse events occurred in 2 (4.17%) and 14 (4.42%) patients in the ILD and N groups, respectively (Figure 1b). No pulmonary complications occurred after ABT administration in the ILD group, but 2 patients in N group had interstitial pneumonia. Treatment was discontinued due to insufficient response in 7 (14.6%) and 38 (12.0%) patients in the ILD and N groups, respectively. None of these were significantly different by group. Mean DAS28-CRP significantly improved in both groups (Figure 2), from 4.7 at ABT initiation to 3.2 at 52 weeks in the L group ($P<0.001$), and from 4.3 to 3.0 in the N group ($P<0.001$). Achievement of those with low disease activity also increased, from9.1% at ABT initiation to 41.8% at 52 weeks in the ILD group, and from 10.7% to 45.5% in the N group.

Conclusions: The safety, treatment effects, and continuation rates of ABT were similar among RA patients with and without interstitial lung disease. Because of pulmonary complications, MTX concomitant rate of ILD group was significantly lower than that of N group. It was reported that

the influence of concomitant MTX in ABT therapy is small. Thus ILD group would have been able to obtain the similar effects to N group. Use of ABT is beneficial even in patients with pulmonary complications, under close consideration of the risks involved.

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座長・司会（医局）

＜リウマチ科＞

No.	演　　題　　名	座長名	学会・研究会名	発表年月日
1	関節リウマチ治療における薬物治療の実際～MTXからBioまで～（小嶋俊久先生）	平野　裕司	第６回　東三河アクテムラカンファランス	2015/2/7
2	生物学的製剤を投与している関節リウマチ患者のインフルエンザワクチンの抗体価についての検討（石川尚人先生）	平原　慎也	RA Nurse Seminar	2015/3/7
3	生物学的製剤とテリパラチド連日投与製剤の併用が関節リウマチ患者の骨密度と骨代謝マーカーにあたえる影響（竹本元大先生）	平野　裕司	第14回東海骨・関節疾患研究会	2015/3/19
4	関節リウマチの骨粗鬆症－IORRAコホートからの検討－（古谷武史先生）	平野　裕司	第３回三河骨粗鬆症研究会	2015/3/21
5	関節リウマチの治療目標を求めて（金物壽久先生）	平野　裕司	第３回三河Orthopaedic Rheumatology研究会	2015/6/27
6	主題　バイオ導入後のRA手術の変化（小山賢介先生、浅井秀司生成、佐久間陸友先生）	平野　裕司	第27回日本リウマチ学会中部支部学術集会	2015/9/4
7	継続率からみたイグラチモドの有効性と安全性について～TBCR plus登録症例における検討～（金山康秀先生）他	平野　裕司	第30回日本臨床リウマチ学会	2015/11/22
8	RA診療における関節エコーの有用性とその実際（松下功先生）	平野　裕司	第2回三河関節エコー研究会	2015/11/28

論文・著書 (医局)

＜リウマチ科＞

No.	題　　名	区分	氏名	著　　書　　名
1	関節リウマチ患者に対する人口膝関節置換術の効果の分析－局所的効果、全身的疾患活動性、生活の質への影響の比較－	筆頭著者	岡田　貴士	日関病会誌. 2015; 34: 45-50.
2	関節リウマチにおける継続率からみたBIOの長期予後の検討	筆頭著者	平野　裕司	中部リウマチ. 2015; 45: 7-10.
3	妊娠後の関節リウマチ患者にセリトリズマブ・ペゴルを投与した一例	筆頭著者	宮入　祐一	中部リウマチ. 2015; 45: 34-36.