Livret GEM N° 1

Septembre 2014

Lyon, juin 2014, GEM3 et les partenaires de Resopso

Mot du président

Chères consœurs, chers confrères

Chers amis

Voilà trois ans que notre groupe de recherche GEM RESOPSO a été créé à l'initiative de François Maccari. J'ai un souvenir précis de la première réunion de création du GEM. François avait proposé que cette nouvelle structure fonctionne à la façon d'une tribu indienne. Le moins de rigidité et de chef possible. Un groupe de dermatologues œuvrant en toute égalité, uniquement porté par l'objectif de faire avancer le projet scientifique d'un des leurs et le savoir commun. Beaucoup à l'issue de la réunion, et j'en étais, ont dû être dubitatifs face à ce projet un brin utopiste.

Il faut croire que l'utopie portée par l'enthousiasme fonctionne. Nous avons fait bien du chemin depuis et le rêve s'est inscrit dans le réel.

Le GEM est une structure originale. Créée ex nihilo, en dehors de toute racine hospitalière ou universitaire, reposant uniquement sur la solidarité et confraternité de ses membres, le GEM est pourtant fondé sur un socle solide : notre curiosité scientifique. Car c'est bien dans notre appétit commun de savoir que réside la clé de notre succès. Et la nécessité bien comprise de fédérer nos forces pour y parvenir. Le GEM a notamment permis à tous ceux comme moi qui n'ont pas d'obligation de recherche de se rattacher à des projets ambitieux et parfois d'en développer.

Nous pouvons tous être fiers d'avoir mené à terme des études d'envergure ayant inclus plusieurs milliers de patients. Le GEM est devenue une entité regardée avec attention et respect par les autres sociétés savantes et les partenaires de l'industrie. Cela nous confère un devoir. Celui de rechercher toujours plus avant l'excellence. Le GEM cube, structure légère d'incubation et d'aide à la promotion des études en cours et à venir a ainsi été créée. A l'issue de la dernière réunion lyonnaise nous avons souhaité réaliser ce livret du GEM que vous tenez en main comme outil d'information de toute la vie du groupe.

Pour conclure j'ai le sentiment que RESOPSO et le GEM sont allés bien au-delà de ce projet de recherche psoriasis. En créant un espace de rencontre confraternel à travers toute la France, en multipliant les rencontres à l'occasion de nos réunions et des congrès, en mettant en avant les valeurs de respect mutuel et d'équité, nous avons renforcé le lien professionnel entre dermatologues. Des liens précieux sont nés, pour beaucoup d'amitié. Nous avons chacun été moins isolés au sein de notre département, de notre cabinet ou de notre hôpital. Ce lien associatif est une vraie richesse. Alors que vive le GEM et bonne lecture….

Edouard Begon
Président de Resopso

Sommaire

RESOPSOCAR

« Psoriasis de l'enfant et facteurs de risque cardio-vasculaire »

Investigateur principal : Emmanuel Mahé, Hôpital Victor Dupouy, Argenteuil.
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Résumé

Le psoriasis touche 2 à 4% de la population générale. Les études épidémiologiques montrent qu'environ 1/3 des cas débutent dans l'enfance (jusqu'à 2/3 dans les formes familiales).
Depuis une dizaine d'années, il a été clairement démontré que le psoriasis chez l'adulte est associé de façon significative au syndrome métabolique et à une augmentation de la fréquence des facteurs de risque cardio-vasculaire, en général : HTA, obésité, diabète, tabagisme, alcoolisme, accidents cardiovasculaires majeurs (AVC, angor, IDM) ainsi qu'à une surmortalité cardiovasculaire.

Les études sur le lien entre psoriasis de l'enfant et facteurs de risque cardio-vasculaire sont rares et contradictoires :

- Une étude récente (de Jager M, et al. JEADV 2010), suggère sur la base d'un questionnaire adressé aux patients de l'association de patients psoriasiques néerlandais (taux de réponse faible : 1/3) qu'un début précoce du psoriasis n'est pas associé à une obésité à l'âge adulte. Les autres pathologies du syndrome métabolique n'ont pas été incluses dans cette étude.
- Une étude allemande suggère que les enfants atteints de psoriasis seraient plus souvent hypertendus, diabétiques, dyslipidémiques, ou victimes d'accidents vasculaires sévères que les enfants non atteints de psoriasis (Augustin M, et al. BJD 2010)

Nous souhaitions donc évaluer le lien entre début du psoriasis dans l'enfance et facteurs de risque cardio-vasculaire (incluant le syndrome métabolique) à l'âge adulte.

L'objectif principal de ce travail était de rechercher si un début précoce du psoriasis, dans l'enfance, est prédictif ou protecteur pour les facteurs de risque cardio-vasculaire à l'âge adulte.
Les objectifs secondaires étaient : évaluer la prévalence des facteurs de risque cardio-vasculaire et du syndrome métabolique dans la population psoriasique française ; analyse en sous-groupes : en fonction du sexe, de l'âge de début (<10 ans / > 10 ans), de la sévérité du psoriasis (évalué sur l'utilisation de traitements généraux), type de psoriasis, antécédents familiaux

Nombre de centres : 29
Nombre d'inclusions : 2 210

Début de l'étude : Juin 2011
Fin de l'étude : Octobre 2011

Présentations : *4 saisons de la Dermatologie, Paris, 2012 ; 2012 Dermatology European Faculty Forum Amsterdam, Pays-Bas, 2012 ; Journées Dermatologiques de Paris, 2012 ; 4th Congress of the Psoriasis International Network - Psoriasis 2013, Paris, 2013 ; 12th World Congress of Pediatric Dermatology, Madrid, Espagne, 2013 ; Journées Dermatologiques de Paris, 2013*

Publications :

Mahé E, Maccari F, Beauchet A, Lahfa M, Barthelemy H, Reguiaï Z, Beneton N, Estève E, Chaby G, Ruer-Mulard M, Steiner HG, Pauwels C, Avenel-Audran M, Goujon-Henry C, Descamps V, Begon E, Sigal ML, for the GEM Resopso. Childhood onset psoriasis: association with future cardiovascular and metabolic comorbidities. *Br J Dermatol* 2013;169:889-95.

Descamps V, Mahé E, Maccari F, Begon E, Barthelemy H, Reguiai Z, Bénéton N, Estève E, Chaby G, Ruer-Mulard M, Steiner HG, Thomas-Beaulieu D, Avenel-Audran M, Goujon-Henry C, Sigal ML, Ezzedine K, Beauchet A. Severe androgenetic alopecia as a proxy of metabolic syndrome in male psoriatic patients older than 59 years. *Eur J Dermatol* 2014 Jun 30.

RESOPSO-PI

« Psoriasis : prise de poids sous infliximab »

Investigateur principal : Emmanuel Mahé, Hôpital Victor Dupouy, Argenteuil.
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Résumé

Le psoriasis touche environ 2 à 4% de la population générale. Depuis une dizaine d'année, il est montré que le psoriasis est associé à des comorbidités cardiovasculaires et métaboliques et notamment l'obésité chez l'adulte et probablement aussi chez l'enfant. La correction des comorbidités cardiovasculaires et métaboliques est devenue un sujet de préoccupation des dermatologues prenant en charge les patients psoriasiques.

L'impact des traitements systémiques et notamment des biologiques, sur l'amélioration des comorbidités, est le sujet de plusieurs publications mais aussi un enjeu commercial non négligeable.

Le TNF alpha est impliqué dans la physiopathologie du psoriasis. Il est aussi impliqué dans l'homéostasie du poids : il favorise la lipolyse et le catabolisme musculaire. Les anti-TNF alpha, l'étanercept (Enbrel®), l'adalumimab (Humira®) et l'infliximab (Remicade®) sont utilisés de plus en plus souvent dans la prise en charge des patients présentant un psoriasis en plaques modéré à sévère (30% des patients dans l'étude Resopsocar). Récemment plusieurs études ont montré que ces traitements induisent une augmentation pondérale chez les patients traités pour des affections rhumatologiques ou dermatologiques, prise de poids qui ne serait pas observée chez les patients sous méthotrexate.

Deux travaux récents, français, ont cherché à identifier des facteurs de risque de prise pondérale chez ces patients avec des résultats contradictoires :

- Florin V, ET AL. Prise de poids sous infliximab : étude rétrospective à propos de 35 malades. Ann Dermatol Venereol 2011 5ABSTRACT jdp°
- Forien M, Mahé E, Sin C, Marchal A, Sigal ML. Variation pondérale chez les patients recevant un traitement systémique pour un psoriasis. Ann Dermatol Venereol 2012

Dans ces 2 travaux, il semble que le poids initial soit un paramètre majeur de variation pondérale à 1 an.

L'objectif de cette étude était d'évaluer dans des conditions « pragmatiques », les facteurs de risque de prise pondérale chez les patients psoriasiques sous infliximab,

Nombre de centres : 19
Nombre d'inclusions : 191

Début de l'étude : Avril 2012
Fin de l'étude : Juin 2012

Présentation : *4th Congress of the Psoriasis International Network - Psoriasis 2013, Paris, 2013*

Publication :

Mahé E, Reguiai Z, Barthelemy H, Quiles-Tsimaratos N, Chaby G, Girard C, Estève E, Maccari F, Descamps V, Schmutz JL, Begon E, Bravard P, Maillard H, Boyer T, Beauchet A, Sigal ML, for the GEM Resopso. Evaluation of risk factors for body weight increment in psoriatic patients on infliximab: a multicentre, cross-sectional study. *J Eur Acad Dermatol Venereol* 2014;28:151-159.

RESOSWITCH

« Etude des changements d'une biothérapie par une autre pour le traitement du psoriasis »

Investigateur principal : Ziad Reguiai, CHU de Reims
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Résumé

Nombre de centres :
Nombre d'inclusions :

Début de l'étude :
Fin de l'étude :

Présentation : *Journées Dermatologiques de Paris, 2013*

VITIBIO

« Apparition ou modification d'un Vitiligo sous biothérapie »

Investigateur principal : Laure Méry-Bossard, CH François Quesnay, Mantes la Jolie
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Résumé
Il s'agit d'un appel à observation reposant sur la diffusion de cette étude par l'intermédiaire des sites internet respectifs du GEM Resopso, SFD et du CRI.
L'objectif de ce travail est de mieux comprendre les caractéristiques de survenue de troubles pigmentaires ainsi que leur évolution chez des patients sous biothérapies pour les indications suivantes :

- psoriasis cutané et/ou rhumatisme psoriasique
- maladie de Crohn et rectocolite hémorragique
- spondylarthrite ankylosante et autres spondyloarthrites
- polyarthrite rhumatoïde
- ou d'éventuelles indications hors AMM.

Investigateur associé (CRI) : Pr Eric Toussirot, service de rhumatologie, CHRU Besançon

Nombre d'inclusions : 12

Début de l'étude : juillet 2013
Fin de l'étude : décembre 2014

Présentation : *Société Française de Rhumatologie, 2013, EULAR 2014/ ACR 2014*

R-ENS

« Resopso : Evaluation Nationale du parcours de Soin pour un psoriasis »

Investigateur principal : Emmanuel Mahé, Hôpital Victor Dupouy, Argenteuil.
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Résumé

Si le psoriasis est considérée comme bénin, car non mortel, par beaucoup, sa sévérité potentielle et son retentissement sont finalement admis actuellement à plusieurs niveaux :

- physique : certaines formes cliniques présentent un retentissement fonctionnel (acropulpites, psoriasis palmoplantaire par exemple), général (érythrodermie, psoriasis pustuleux), et social (psoriasis du visage, psoriasis unguéal) majeur
- la qualité de vie (QDV) : il n'est plus à démontrer que les différentes dimensions de la qualité de vie sont impactées par le psoriasis (travail, vie familiale, sexualité, ….)
- social : altération des activités collectives, professionnelles, familiales, sportives par exemple
- économique : coût directs (ex : traitements et hospitalisation) et indirects (arrêts de travail, dépressions induites …)
- enfin l'association du psoriasis aux comorbidités métaboliques et cardiovasculaires fait parler par certains auteurs de « maladie systémique »

Paradoxalement, tant en pratique clinique que dans les données de la littérature, il est montré que :

- une minorité de patients est prise en charge
- la prise en charge des formes sévères est très (trop ?) tardive
- une prise en charge adaptée améliore les différentes dimensions altérées : physique, QDV, social

Peu d'informations sont disponibles pour essayer d'expliquer les raisons de ce retard de prise en charge, où pourquoi les patients tardent tant pour être pris en charge ? S'agit-il de données médicales (par exemple : sous-évaluation du retentissement par le médecin), sociales comme observées pour certaines pathologies comme les cancers ou les maladies cardiovasculaires (rapidité de prise en charge et pronostic corrélé de façon inverse au statut social), individuelles (ex : hommes moins préoccupés par leur apparence que les femmes, …) …

L'objectif de ce travail était de mieux comprendre le parcours des patients psoriasiques avant de consulter un dermatologue adhérent à un réseau de praticiens investis dans la prise en charge du psoriasis, hospitaliers ou libéraux, chez les patients psoriasiques primo-consultants.

Nombre de centres : 40
Nombre d'inclusions : 1 302

Début de l'étude : 1er janvier 2013
Fin de l'étude : 15 novembre 2013

Présentations : *Journées Dermatologiques de Paris 2013 ; 11th EADV Spring Symposium, Belgrade, Serbie, 2014*

METHOPRAC

« Enquête observationnelle multicentrique pour évaluer l'utilisation du METHOtrexate en PRAtique Courante dans le psoriasis en plaques »

Investigateur principal : Abdallah Khemis, CHU Nice
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Résumé

Rationnel :
- Utilisation croissante du méthotrexate depuis l'émergence des biothérapies
- Aucune étude prospective de grande envergure pour ce médicament incontournable dans le psoriasis
- Absence de recommandation sur l'utilisation optimale du méthotrexate

Objectif principal :
- Efficacité du méthotrexate en terme de PASI 75 à 16 semaines de traitement

Objectif secondaire :
- Efficacité du méthotrexate en terme de PASI 75 à 12 semaines de traitement
- Tolérance en fonction des posologies (15mg/semaine versus 20mg/semaine) et des voies d'administration (per os versus sous-cutané)
- Efficacité à la semaine 12 et à la semaine 16 en termes de PASI 50 et PASI 90
- Impact de l'utilisation de la Spéciafoldine
- Délai de réponse
- Evaluation de la compliance et de l'observance
- Evaluation de l'efficacité et de la tolérance à 6 mois

Nombre de centres : 19
Nombre d'inclusions : 144 (30/08/2014)

Début de l'étude : janvier 2014
Fin de l'étude : février 2015

MGUS

« Apparition de gammapathies monoclonales dans le psoriasis sous biothérapie »

Investigateur principal : Anne-Laure Liégeon, Jean-Luc Schmutz, CHU Nancy, Vandœuvre-Les-Nancy
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Résumé

Le psoriasis est une maladie inflammatoire chronique dont la prévalence est estimée à 1,5% à 3% de la population générale. La prise en charge s'est vue modifiée ces dernières années avec l'apparition des nouvelles thérapeutiques : les biothérapies. Les principaux effets secondaires connus sont infectieux et cancéreux. L'impact de ces traitements est toujours en cours d'évaluation.

Une étude Italienne récente a montré l'apparition de gammapathie monoclonale bénigne chez 12 patients après 8 mois de traitement par efalizumab. La régression était spontanée après l'arrêt du traitement. Une seconde étude à plus grande échelle, menée par l'équipe du docteur Prignano et comprenant 300 patients a permis de confirmé cette découverte. Huit patients sur 300 ont développé une gammapathie monoclonale ou une double gammapathie monoclonale. Le diagnostic de gammapathie monoclonale bénigne était retenu. Le délai d'apparition variait de 9 à 16 mois.

L'électrophorèse des protéines sériques est recommandée dans le bilan pré thérapeutique. Le suivi biologique des patients sous biothérapie se fait selon l'appréciation du médecin. Les habitudes sont variables, mais un bilan sanguin est souvent réalisé tous les quatre semaines à quatre mois. Le but du bilan est de contrôler la tolérance du traitement et de rechercher un point d'appel infectieux voire cancéreux. L'électrophorèse des protéines sériques est un examen couramment prescrit permettant de rechercher un syndrome inflammatoire et une gammapathie monoclonale, souvent premier signe d'une maladie de la lignée sanguine. Lorsque l'on découvre une gammapathie monoclonale, le diagnostic de gammapathie monoclonale bégnine ou MGUS (*monoclonal gammapathy of undertermined snifiance*) est retenue dans 65% des cas. Cette pathologie est fréquente, puisqu'elle atteint 1% de la population à 60 ans, 3% à 70 ans et 10% à 80 ans. Le risque de dégénérescence est non négligeable, 10% de transformation maligne à 10 ans.

Certaines affections sont associées à une gammapathie monoclonale. Le psoriasis n'en fait pas partie même si l'on suppose, du fait de son mécanisme inflammatoire, qu'il existe une augmentation de la proportion des gammapathies monoclonales dans cette population. Enfin certaines thérapeutiques sont connues pour donner des gammapathies monoclonales mais jusqu'à présent les biothérapies n'en faisaient pas parties.

Hypothèses de recherche : Suite aux découvertes Italienne, il parait nécessaire de réaliser une étude Française afin de confirmer les résultats concernant l'apparition de gammapathie monoclonale. Si cela se confirmait, il faudrait modifier les modalités de surveillance des traitements sous biothérapie et imposer la réalisation d'une électrophorèse des protéines sériques. Les gammapathies monoclonales sont révélateurs de plusieurs pathologies à caractères malins ou à fort potentiel de dégénérescence.

Objectif Principal : Déterminer la prévalence des gammapathies monoclonales sous biothérapie

Nombre de centres : 16
Nombre d'inclusions : 445

Début de l'étude : 1er août 2013
Fin de l'étude : 31 juillet 2014

RESOPSONET

« Patients souffrant de psoriasis et internet »

Investigateur principal : Maud Amy de la Bretèque, Hôpital Victor Dupouy, Argenteuil.
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Résumé

En France un peu plus de trois personnes sur quatre ont globalement accès à internet, mais le pourcentage d'internautes dans la population est plus élevé chez les plus jeunes, de 99% chez les 12-17ans à 22% des plus de 70 ans. Selon la revue de la littérature « Le patient internaute », élaborée par la HAS, 1 patient sur 5 environ cherche de l'information médicale et de santé sur Internet. Les résultats de l'enquête Médiamétrie/Net Ratings indiquent par ailleurs que, parmi les 25 sites les plus visités en France au mois de septembre 2007, figurent deux sites Internet santé ou site disposant d'un espace d'information dédiée à l'information santé.

Ces données témoignent de la montée en puissance du media Internet dans le traitement des sujets médicaux et de santé. En effet, les patients n'hésitent plus à multiplier leurs sources d'information santé et à les recouper, y compris sur Internet.

Concernant l'utilisation d'internet chez des patients atteints de psoriasis, des travaux ont été publiés sur l'utilisation des réseaux sociaux. Les auteurs ont montré que ces communautés virtuelles offraient aux utilisateurs à la fois une valeur éducative et un soutien psychologique et social (*Arch Dermatol 2009)*.

Il est légitime de s'interroger sur le profil des patients qui cherchent ce type d'information et sur la qualité de cette information.

L'objectif de cette étude est de décrire les caractéristiques des patients atteints de psoriasis consultant internet, de décrire le contexte et l'impact de ces recherches sur le comportement des patients. Dans un second temps, les sites les plus visités seront analysés avec évaluation des critères de qualité des sites, et de la qualité de l'information médicale.

Nombre de centres : 38
Nombre d'inclusions : 115 (au

Début de l'étude : 25 août 2014
Fin de l'étude : En cours. Date prévue de fin d'étude : 31 octobre 2014 (arrêt de l'étude à 1000 inclusions)

CIRRHOSE - BIO

« Etude rétrospective de la tolérance et de l'efficacité des biothérapie dans le psoriasis chez les patients cirrhotiques post alcooliques »

Investigateur principal : Edouard BEGON, Hôpital René Dubos, Pontoise.
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Résumé

L'objectif est d'analyser de façon rétrospective en premier lieu la tolérance et en second lieu l'efficacité des médicaments biologiques du psoriasis chez les patients psoriasiques présentant une cirrhose alcoolique.

Les données de tolérance et d'efficacité des biologiques du psoriasis ont été largement analysées au travers d'études prospectives et d'étude de cohorte. Ces mêmes données restent cependant parcellaires dans des populations présentant des comorbidités spécifiques. Ces patients sont le plus souvent exclus des essais thérapeutiques et des cohortes prospectives post essais de phase III. La tolérance des traitements en vie réelle reste donc mal appréciée. La tolérance et l'efficacité des biologiques dans la population des patients psoriasiques et cirrhotiques post alcooliques n'a jamais été étudiée. De rares cas cliniques sont retrouvés dans la littérature mais aucune série ne s'est intéressée à ce sujet. L'indication des biologiques est pourtant réelle dans cette population présentant souvent un psoriasis étendu / sévère où les autres systémiques sont le plus souvent contre indiqués ou difficiles d'utilisation (hépatotoxicité rétinoïdes et méthotrexate, contre-indication de la méladinine, mauvaise observance). De plus les biologiques ne sont pas hépatotoxiques et sont compatibles pharmacologiquement avec l'insuffisance hépatocellulaire. Bien que plusieurs études aient mis en évidence l'effet délétère du TNF dans la progression de l'hépatite alcoolique et que certains auteurs aient proposé dans le passé l'emploi des anti TNF en cas d'hépatite alcoolique aigue la littérature ne donne aucun renseignement fiable quant à l'utilisation des biologiques en cas de cirrhose. Certaines séries hépatologiques d'hépatite alcoolique aigue traitée par infliximab ont montré un risque infectieux notable.

L'étude vise à inclure tous les patients présentant une cirrhose post alcoolique (± association à une stéatohépatite dysmétabolique ou NASH) atteint d'un psoriasis cutané ± articulaire et ayant reçu au moins une dose d'une biothérapie anti TNF ou anti Il 12/23 (infliximab, adalimumab, étanercept, ustekinumab). Le diagnostic de cirrhose post alcoolique devra avoir été défini par un hépatologue selon les critères professionnels retenus (la preuve histologique n'est pas nécessaire). L'étude exclut les autres causes d'hépatopathie : fibrose hépatique sans cirrhose, hépatite virale chronique active ou guérie, autre pathologie hépatique concomitante ou passé (auto-immune, CBP..).

L'objectif premier de cette étude rétrospective est d'étudier la tolérance des biothérapies dans cette population. Le risque infectieux accru, le risque néoplasique (carcinome hépato cellulaire) voire un risque d'aggravation de la cirrhose (survenue de complications liées à la cirrhose) sont notamment les points déterminants à analyser. L'objectif second est d'analyser l'efficacité des biologiques.

Nombre de centres sollicités : 56

Début de l'étude : septembre 2014
Fin de l'étude : mai 2015

RESOPSO SENIOR

*« **S**afety and efficacy of biologic treatments in **E**lderly patie**N**ts with psor**I**asis: a multicenter nati**O**nal ret**R**ospective study »*

Investigateurs : Nathalie Beneton, CH Le Mans
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Résumé

L'étude a pour objectifs :

Objectif primaire :
Etude la tolérance des biologiques chez patients atteints de psoriasis de plus de ≥ 65 (inclus)

Objectifs secondaires :
Etude de l'efficacité des biologiques chez ces patients
Description des caractéristiques phénotypiques du psoriasis et les comorbidités

Critères d'inclusion :

Inclusion des patients ayant 65 ans ou plus lors de l'initiation ou survenant au cours d'un traitement par biologique prescrit pour un psoriasis cutané : étanercept, adalimumab, infliximab, ustekinumab. Il peut s'agir de patients naïfs ou non de biologiques antérieurs.

Nombre de centres sollicités : 56

Début de l'étude : 30 septembre 2014
Fin de l'étude : 31 janvier 2015

Présentations aux congrès

4 SAISONS DE LA DERMATOLOGIE, PARIS, 2012

ETUDE RESOPSOCAR : LE DEBUT D'UN PSORIASIS DANS L'ENFANCE AUGMENTE-T-IL LA FREQUENCE DES FACTEURS DE RISQUE CARDIOVASCULAIRE A L'AGE ADULTE ? RESULTATS PRELIMINAIRES
Mahé E, Maccari F, Barthelemy H, Reguiai Z, Estève E, Beneton N, Maillard H, Chaby G, Ruer-Mulard M, Steiner HG, Lahfa M, Begon E, Pauwels C, Avenel-Audran M, Goujon-Henry C, Descamps V, Beauchet A, Sigal ML, pour le GEM RESOPSO.

2012 DERMATOLOGY EUROPEAN FACULTY FORUM AMSTERDAM, PAYS-BAS, 2012

PSORIASIS AND CARDIOVASCULAR AND METABILIC COMORBIDITIES: IMPORTENCE OF THE CENTER EFFECT.
Mahé E, Barthélémy H, Reguiai Z, Chaby G, Estève E, Beneton N, Maillard H, Ruer-Mullard M, Beauchet A, Lahfa M, Maccari F, Sigal ML, for the GEM RESOPSO.

PSORIASIS AND NICOTINE ADDICTION IN FRANCE
Mahé E, Barthélémy H, Maccari F, Beauchet A, Lahfa M, Reguiai Z, Estèves E, Beneton N, Maillard H, Chaby G, Ruer-Mullard M, Steiner HG, Pauwels C, Avenel-Audran M, Goujon-Henry C, Descamps V, Begon E, Sigal ML, for the GEM RESOPSO.

JOURNEES DERMATOLOGIQUES DE PARIS, 2012

ETUDE RESOPSOCAR : LE DEBUT D'UN PSORIASIS DANS L'ENFANCE N'INFLUENCE PAS LA FREQUENCE DES FACTEURS DE RISQUE CARDIOVASCULAIRE A L'AGE ADULTE
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ALOPECIE ANDROGENETIQUE MASCULINE AU COURS DU PSORIASIS : UN MARQUEUR DU SYNDROME METABOLIQUE ?
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EVALUATION OF RISK FACTORS FOR BODY WEIGHT GAIN IN PSORIATIC PATIENTS ON INFLIXIMAB: A MULTICENTRE, CROSS-SECTIONAL STUDY
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CHILDHOOD ONSET PSORIASIS AND ITS DURATION: ASSOCIATION WITH FUTURE CARDIOVASCULAR AND METABOLIC DISEASES
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LA SEVERITE DU PSORIASIS LORS D'UNE PREMIERE CONSULTATION EN DERMATOLOGIE EST-ELLE CORRELEE AU STATUT SOCIOECONOMIQUE DU PATIENT ?
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NEW ONSET VITILIGO UNDER BIOLOGOICAL AGENTS: A CASE SERIE
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IS SEVERITY OF PSORIASIS, AT THE FIRST CONSULTATION IN A DERMATOLOGY DEPARTMENT, CORRELATED TO THE SOCIO- ECONOMIC PROFILE OF THE PATIENT?
Mahé E, Maccari F, Quiles-Tsimaratos N , Reguiai Z, Le Guyadec T, Estève E, Ruer-Mulard M, Chaby G, Barthelemy H, Maillard H, Parier J, Steiner HG, Schmutz JL, Girard C, Bégon E, Beauchet A, Sigal ML, GEM RESOPSO.

IS THERE A DERMATOLOGICAL "WANDERING" BEFORE A FIRST CONSULTATION FOR PSORIASIS IN A DEPARTMENT OF DERMATOLOGY?
Mahé E, Maccari F, Quiles-Tsimaratos N, Reguiai Z, Le Guyadec T , Estève E , Ruer-Mulard M, Chaby G, Barthelemy H, Maillard H, Parier J, Steiner HG, Schmutz JL, Girard C , Begon E, Beauchet A , Sigal ML, GEM RESOPSO.

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Childhood-onset psoriasis: association with future cardiovascular and metabolic comorbidities

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Summary

Background Psoriasis is associated with higher prevalences of cardiovascular and metabolic comorbidities in adults but the relationship of age at onset and those prevalences is unknown.
Objective To evaluate whether the childhood onset of psoriasis (COP) is correlated with the frequency of cardiovascular and metabolic comorbidities in adulthood.
Methods This noninterventional, cross-sectional, multicentre study of adults with psoriasis was conducted in 29 dermatology centres in France. Data on sex, age at onset of psoriasis and its clinical characteristics, and cardiovascular risk factors, including weight, body mass index, waist circumference, dyslipidaemia, diabetes, hypertension, smoking, and personal/familial major adverse cardiovascular events (MACE) were systematically recorded.
Results Two thousand two hundred and one patients with psoriasis (male: 56%; mean age: 49 years; 25% with COP) were included consecutively in the study. Univariate analysis showed that COP was associated with lower frequencies of obesity, high waist circumference, diabetes, dyslipidaemia, hypertension, familial cardiovascular disease, MACE and metabolic syndrome, but more frequent active smoking. Multivariate analysis retained age as being associated with frequency of cardiovascular and metabolic comorbidities, and sex with smoking, but not age at the onset of psoriasis. Psoriasis severity was associated with higher frequencies of obesity and psoriatic arthritis.
Conclusion Our results showed that COP does not seem to be an additional risk factor for higher frequencies of cardiovascular and metabolic comorbidities during adulthood.

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What's already known about this topic?

- Psoriasis and its severity are associated with higher prevalence of cardiovascular and metabolic comorbidities in adults.
- Childhood onset of psoriasis is not associated with obesity in adulthood.

What does this study add?

- Childhood onset of psoriasis is not associated with cardiovascular and metabolic comorbidities in adulthood.
- In France, as in most countries, psoriasis is associated with high frequencies of cardiovascular and metabolic comorbidities in adults.

Psoriasis is a chronic immune-mediated inflammatory disorder affecting 2–3% of the white population in western countries.[1] During the past decade, cardiovascular, i.e. hypertension, coronary diseases, major cardiovascular events (MACE), and metabolic, i.e. obesity, abnormal plasma lipid metabolism, and insulin resistance, comorbidities have been associated with psoriasis.[2–8] Smoking and parental cardiovascular diseases, two major risk factors for cardiovascular diseases, are also associated with psoriasis.[9–11] The notion of a psoriatic march is debated.[8,12–15] The hypothesis of an aetiological role of psoriasis in cardiovascular and metabolic diseases is supported by pathogenic concepts establishing a link between chronic inflammation in psoriasis, insulin resistance, endothelial cell dysfunction and atherosclerosis.[12,16–19]

The childhood onset of psoriasis (COP) is relatively common. According to the literature, 35–50% of patients with psoriasis have the disease before the age of 20 years[1,20–22] and in Europe about 1% of children are affected.[14,23] Some studies also show that children with psoriasis have higher risks for cardiovascular and metabolic comorbidities.[23,24] Little information is available about the link between COP and cardiovascular and metabolic diseases in adulthood. Recently the authors of one study found that COP did not influence future body mass index (BMI).[25]

Therefore, we conducted a multicentre cross-sectional study to evaluate the potential relationship between age at the onset of psoriasis and the patients' frequencies of cardiovascular risk factors, and cardiovascular and metabolic diseases during adulthood.

Methods

This noninterventional, cross-sectional, multicentre study of adults with psoriasis was performed in 29 dermatology centres in France from 15 June to 31 October 2011. COP was defined as disease onset before the age of 18 years, and adult-onset psoriasis (AOP) as disease onset after 18 years.

Investigative centres

Twenty-nine dermatological centres throughout France, members of Resopso, participated in this study. Resopso (http://resopso.fr) is an association of French dermatologists involved in the care of patients with psoriasis. These 29 centres were in university (n = 9), general (n = 11) and military hospitals (n = 2), and with private practitioners (n = 7). Seven had clinics dedicated to patients with psoriasis.

Patient evaluation

All patients with psoriasis who had a consultation during the 4·5 months of the study in the 29 centres were included in the study. A protocol for evaluation was implemented with a case report form especially created for the study. It comprised 38 items, including data on patients (i.e. age, sex); psoriasis (i.e. age at onset, clinical characteristics, rheumatism, history of treatments, family history including first-degree relatives only); cardiovascular risk factors and diseases (i.e. hypertension, current smoking, MACE (including angina pectoris, myocardial infarction and stroke) and family history of MACE (including myocardial infarction, cardiac death and stroke in first-degree relatives); and metabolic diseases (i.e. weight, BMI calculated as weight in kg divided by height in m^2, waist circumference, diabetes and dyslipidaemia).

Overweight was defined as a BMI > 25 kg m^{-2}, and obesity as BMI > 30 kg m^{-2}.[26,27] Diabetes mellitus was diagnosed when patients had a fasting glycaemia ≥ 7 mmol L^{-1} (1·26 mg L^{-1}), or reported the use of oral glucose-lowering medication or insulin. Participants were classified as having hypertension when their systolic blood pressure was ≥ 140 mmHg or diastolic blood pressure was ≥ 90 mmHg, or they reported taking blood pressure-lowering medication. Dyslipidaemia was defined as low-density lipoprotein cholesterol levels ≥ 160 mg dL^{-1} (4·14 mmol L^{-1}), high-density lipoprotein cholesterol levels < 40 mg dL^{-1} (1·03 mmol L^{-1}), and triglyceride levels ≥ 200 mg dL^{-1} (2·26 mmol L^{-1}).

Subjects taking lipid-lowering medication were also classified as having dyslipidaemia. A current smoker was defined as consuming ≥ 5 cigarettes per day for at least 1 year. Metabolic syndrome was diagnosed for patients with three of the following four criteria: waist circumference > 80 cm for females and 94 cm for males (European reference for waist circumference) or BMI ≥ 30 kg m^{-2}; diabetes mellitus; hypertension; and dyslipidaemia.[28] Severe psoriasis corresponds to those patients receiving traditional systemic treatment (i.e. acitretin, methotrexate, ciclosporin) or a biologic, on the day of inclusion in the study.

Statistical analysis

Quantitative data are expressed as means ± standard deviation (SD), qualitative data as n (%). Means were compared using Student's t-test and frequencies with the χ^2 test or Fisher's exact test when necessary. Multiple regression analysis was used to evaluate the relationship between risk factors and the features of psoriasis, the latter being those achieving $P < 0{\cdot}05$ in univariate analysis. Because of multiple comparisons a Bonferroni adjustment was performed. A P value $< 0{\cdot}001$ was considered as statistically significant. Statistical analyses were computed with SAS software v 9.3 (SAS Institute Inc., Cary, NC, U.S.A.).

Results

Among the 2255 psoriatic patients seen in the 29 dermatology centres, 54 were not included because they were < 18 years old at inclusion (n = 5), no information was available about age at inclusion or age at onset of psoriasis (n = 18), or they were duplicates (n = 31). Finally 2201 patients were included.

Patients and the characteristics of psoriasis

The patients' mean age at inclusion was 49 (range 18–97) years and 56% were men (Table 1). The mean age at onset of psoriasis was 31 (range 0–92) years. For 25% of patients, the first signs of the disease occurred before the age of 18 years and this was more frequently seen in women. The mean duration of psoriasis was 18 (range 0–81) years. Affected first-degree relatives were: 25% of parents, 15% of siblings, and 7% of children. Plaque psoriasis was the predominant type, and it occurred significantly more often in males. Other characteristics of these patients and their disease are reported in Table 1.

About one-third of the patients were taking traditional systemic treatments (i.e. acitretin, ciclosporin or methotrexate) on the day of inclusion, and approximately one quarter received a biologic (i.e. etanercept, adalimumab, infliximab or ustekinumab).

Compared with patients with AOP, those with COP were significantly younger. Their mean duration of psoriasis was significantly longer, they had significantly more frequent familial disease, plaque psoriasis, and were more often on treatment with a biologic, but less often on traditional systemic therapy.

Cardiovascular and metabolic diseases

Patients with psoriasis were frequently overweight (including obesity) (58%), diabetic (11%), dyslipidaemic (28%), hypertensive (26%), smokers (33%), and had a familial cardiovascular disease history (24%) (Table 2). The metabolic syndrome was diagnosed in 15% of the patients, and 7% suffered from MACE. Compared with women, men were significantly more often overweight or obese, dyslipidaemic, hypertensive, current smokers and had MACE.

According to our univariate analysis, comparing COP vs. AOP patients, patients with COP weighed significantly less, with significantly lower BMI, waist circumference, and frequency of overweight and obesity, diabetes, dyslipidaemia, hypertension and family history of cardiovascular diseases, but they were more frequently smokers. MACE and metabolic syndrome showed similar tendencies, being significantly more frequent in AOP patients than in COP subjects.

Multivariate analyses

Our multivariate analyses (Table 3) retained age as significantly associated with waist circumference, and higher frequencies of obesity, diabetes, dyslipidaemia, hypertension and psoriatic arthritis with a lower percentage of smokers. Also there was a significantly higher frequency of smokers among males. These analyses showed the severity of psoriasis to be significantly associated with a higher frequency of obesity and psoriatic arthritis. Finally, age at the onset of psoriasis had no effect on the frequencies of metabolic and cardiovascular comorbidities.

Discussion

This multicentre study of 2201 French patients with psoriasis was undertaken to examine the potential relationship between age at the onset of psoriasis on the frequencies of cardiovascular and metabolic comorbidities in adulthood. Our results showed, in accordance with an earlier report that found COP to have no influence on the frequency of obesity in adulthood,[25] that age at onset was not associated with adult frequencies of comorbidities. Finally, the only parameter that modified frequencies of comorbidities was the age of the patient, with the exception of smoking for which male gender was an independent parameter associated with a higher frequency of smoking.

Comparing COP with AOP provided more information on the relationship between the age at onset of psoriasis and the disease course. Consistent with earlier studies, COP was more frequent in girls,[22,25,29] and was associated with a family history of psoriasis,[20,22,29,30] but not with joint involvement.[29–31] Our findings also showed that age at the onset of psoriasis had no relationship with disease severity. No consensus has been

Table 1 Clinical characteristics at inclusion of the 2201 psoriasis patients according to sex, age at onset and disease duration (univariate analysis)

		Sex			Age at onset of psoriasis		
Characteristic	All patients n = 2201	Male n = 1240	Female n = 961	P-value	COP[a] n = 545	AOP[a] n = 1656	P-value
Age (years), mean ± SD	48·7 ± 15·5	48·7 ± 14·5	48·6 ± 16·6	NS	39·1 ± 13·5	51·8 ± 14·8	< 0·0001
Sex, male/female	1240/961	NA	NA	NA	260/285	980/676	< 0·0001
Age (years) at onset of psoriasis, mean ± SD	31·1 ± 17·5	31·3 ± 16·3	30·9 ± 18·8	NS	11·6 ± 4·4	37·5 ± 15·3	NA
Onset before 18 years, n (%)	545 (24·8)	260 (21·0)	285 (29·7)	< 0·0001	545 (100)	0	NA
Psoriasis duration (years), mean ± SD	17·6 ± 13·7	17·4 ± 13·1	17·7 ± 14·5	NS	27·5 ± 13·7	14·3 ± 12·0	< 0·0001
Familial psoriasis, n (%)[b]	867 (40·0)	481 (39·5)	386 (40·8)	NS	293 (54·7)	574 (35·2)	< 0·0001
Plaque psoriasis, n (%)	1633 (78·9)	990 (85·1)	643 (71·1)	< 0·0001	449 (87·2)	1184 (76·2)	< 0·0001
Joint involvement, n (%)	419 (21·5)	221 (20·2)	198 (23·2)	NS	96 (19·9)	323 (22·0)	NS
Treatment of psoriasis, n (%)							
None	111 (5·3)	61 (5·2)	50 (5·5)	0·0007	26 (5·1)	85 (5·4)	< 0·0001
Topical	940 (44·8)	500 (42·3)	440 (48·0)		186 (36·2)	754 (47·6)	
Phototherapy	85 (4·0)	54 (4·6)	31 (3·4)		21 (4·1)	64 (4·0)	
Traditional systemic	747 (35·6)	411 (34·8)	336 (36·6)		163 (31·7)	584 (36·8)	
Biologic	683 (32·5)	432 (36·5)	251 (27·4)		206 (40·1)	477 (30·1)	
Severe psoriasis, n (%)[c]	1437 (65·3)	848 (68·4)	589 (61·3)	0·0005	374 (68·6)	1063 (64·2)	NS

NS, not significant; NA, not applicable. [a]Childhood-onset psoriasis (COP) was defined as disease onset before the age of 18 years, and patients with adult-onset psoriasis (AOP) as disease onset after 18 years. [b]Familial psoriasis was defined as psoriasis occurring in first-degree relatives: parents (n = 550), brothers/sisters (n = 329), and/or children (n = 147). [c]Severe psoriasis corresponds to patients receiving traditional systemic treatment (i.e. acitretin, methotrexate, ciclosporin), or a biologic the day of inclusion in the study.

Table 2 Cardiovascular disease, its risk factors and metabolic diseases according to sex, age at psoriasis onset and its duration (univariate analysis)

		Sex			Age at psoriasis onset		
Characteristics	All the patients n = 2201	Male n = 1240	Female n = 961	P-value	COP[a] n = 545	AOP[a] n = 1656	P-value
Weight (kg), mean ± SD	77·7 ± 18·0	83·6 ± 16·4	70·0 ± 17·0	< 0·0001	74·2 ± 17·8	78·8 ± 17·9	< 0·0001
BMI (kg m^{-2}), mean ± SD	27·0 ± 5·8	27·3 ± 5·1	26·7 ± 6·5	NS	25·8 ± 5·8	27·4 ± 5·7	< 0·0001
< 25, n (%)	917 (42·0)	443 (36·0)	474 (49·7)	< 0·0001	280 (51·8)	637 (38·7)	< 0·0001
25–29·9, n (%)	734 (33·6)	495 (40·2)	239 (25·1)		164 (30·3)	570 (34·7)	
≥ 30, n (%)	534 (24·4)	294 (23·9)	240 (25·2)		97 (17·9)	437 (26·6)	
Waist circumference (cm), mean ± SD	95·9 ± 16·0	98·5 ± 15·0	92·5 ± 16·6	< 0·0001	91·5 ± 15·7	97·3 ± 15·9	< 0·0001
Diabetes, n (%)	238 (10·9)	135 (11·0)	103 (10·7)	NS	25 (4·6)	213 (12·9)	< 0·0001
Dyslipidaemia, n (%)	599 (27·5)	378 (30·8)	221 (23·2)	< 0·0001	89 (16·4)	510 (31·1)	< 0·0001
Hypertension, n (%)	570 (26·0)	342 (27·7)	228 (23·8)	NS	68 (12·5)	502 (30·5)	< 0·0001
Smoking, n (%)	712 (32·6)	421 (34·3)	291 (30·4)	NS	205 (37·8)	507 (30·9)	NS
Familial cardiovascular history, n (%)	508 (24·4)	281 (24·1)	227 (24·6)	NS	99 (18·9)	409 (26·2)	< 0·0001
MACE, n (%)	143 (6·5)	98 (7·9)	45 (4·7)	NS	14 (2·6)	129 (7·8)	< 0·0001
Angina pectoris	63 (2·9)	44 (3·6)	19 (2·0)	NS	7 (1·3)	56 (3·4)	NS
Myocardial infarction	56 (2·5)	41 (3·3)	15 (1·6)	NS	8 (1·5)	48 (2·9)	NS
Stroke	40 (1·8)	26 (2·1)	14 (1·5)	NS	2 (0·4)	38 (2·3)	NS
Metabolic syndrome, n (%)	318 (15·3)	186 (15·9)	132 (14·6)	NS	39 (7·6)	279 (17·8)	< 0·0001

NS, not significant; BMI, body mass index; MACE, major adverse cardiovascular events. [a]Childhood-onset psoriasis (COP) was defined as disease onset before the age of 18 years, and patients with adult-onset psoriasis (AOP) as disease onset after 18 years.

reached on whether the onset of psoriasis during childhood predicts milder or more severe disease. Some authors found early onset to be associated with greater severity,[29–31] while others reported no influence of age at onset.[25,29] The use of different definitions of early psoriasis or COP and the criteria of severity evaluated [body surface area (BSA), Psoriasis Area and Severity Index (PASI), use of systemic treatment] could explain these differences. For example biologics were prescribed more frequently for patients with COP in our study, probably because of French regulations about their use. The authorization to use

Table 3 Multivariate analysis

Risk factors Psoriasis features	Univariate analysis P-value	Multivariate analysis P-value	 OR (95% CI)
Obesity ($\geq$ 30 kg m^{-2})			
Patient age	< 0·0001	< 0·0001	1·03 (1·02–1·04)
Patient sex	< 0·0001	0·40	–
Age at onset (COP vs. AOP)[a]	< 0·0001	0·37	–
Psoriasis severity[b]	0·0009	< 0·0001	1·56 (1·26–1·98)
Waist circumference			
Patient age	< 0·0001	< 0·0001	1·04 (1·03–1·05)
Patient sex	< 0·0001	0·89	–
Age at onset (COP vs. AOP)[a]	< 0·0001	0·81	–
Psoriasis severity[b]	0·001	0·15	–
Diabetes			
Patient age	< 0·0001	< 0·0001	1·06 (1·05–1·07)
Patient sex	0·66	0·40	–
Age at onset (COP vs. AOP)[a]	< 0·0001	0·11	–
Psoriasis severity[b]	0·65	0·15	–
Dyslipidaemia			
Patient age	< 0·0001	< 0·0001	1·06 (1·05–1·07)
Patient sex	< 0·0001	0·40	–
Age at onset (COP vs. AOP)[a]	< 0·0001	0·11	–
Psoriasis severity[b]	0·65	0·15	–
Hypertension			
Patient age	< 0·0001	< 0·0001	1·08 (1·07–1·10)
Patient sex	0·05	0·005	–
Age at onset (COP vs. AOP)[a]	< 0·0001	0·36	–
Psoriasis severity[b]	0·74	0·08	–
Smoking			
Patient age	< 0·0001	< 0·0001	1·01 (1·007–1·02)
Patient sex	0·04	< 0·0001	1·96 (1·64–2·34)
Age at onset (COP vs. AOP)[a]	0·003	0·23	–
Psoriasis severity[b]	0·003	0·25	–
Psoriasis arthritis			
Patient age	0·001	0·004	–
Patient sex	0·10	0·04	–
Age at onset (COP vs. AOP)[a]	0·35	0·74	–
Psoriasis severity[b]	< 0·0001	< 0·0001	2·33 (1·79–3·02)

OR, odds ratio; CI, confidence interval. [a]Childhood onset psoriasis (COP) was defined as disease onset before the age of 18 years, and patients with adult-onset psoriasis (AOP) as disease onset after 18 years. [b]Severe psoriasis corresponds to patients receiving traditional systemic treatment (i.e. acitretin, methotrexate, ciclosporin), or a biologic the day of inclusion in the study.

a biologic requires the prior administration of at least two conventional systemic treatments, including phototherapy.

Cardiovascular and metabolic comorbidities were very frequent in our population, compared with the French general population. Although our study was not designed to evaluate the frequencies of comorbidities in comparison with the general population, they can be compared with values from databases on the French general population. In 2009, a large cross-sectional study designed to evaluate the frequencies of obesity and comorbidities in 25 286 persons,[32] estimated an obesity rate of 15% for the general population $\geq$ 18 years old. In our study this frequency was higher, 24%. Even if the general population is not strictly comparable for age and sex with our patients with psoriasis, the latter's frequencies were a little higher than those of the general French population, respectively, for hypertension (26% vs. 18%), diabetes (11% vs. 5%), dyslipidaemia (28% vs. 15%) and current smokers (33% vs. 19%).

Of emerging importance is the relationship between cardiovascular and metabolic diseases, and chronic severe psoriasis in adults and children.[33–35] It could explain the higher mortality of patients with severe psoriasis.[2,36,37] However, evaluating the relationship between the severity of psoriasis, its long-term evolution and comorbidities seems quite difficult and open to debate.[14,37] Firstly, severe psoriasis may refer to clinical disease activity and the extent of the lesions as assessed by PASI or BSA as involved;[38] the impact of quality of life, i.e. determination of the Dermatology Life Quality Index score which is not always correlated with clinical severity; some unusual severe forms of psoriasis, such as acrodermatitis; or finally, all patients with psoriasis who require systemic treatment or phototherapy, at any time. Secondly, it is not yet possible to predict the long-term outcome and prognosis of COP, in the absence of prospective long-term evaluation of these children. So, severe psoriasis in childhood can become moderate or mild in adulthood and *vice versa*. Finally, psoriasis is a dynamic disease. Although some patients with psoriasis have long-term severe disease, others have transient severe disease, e.g. sometimes triggered by stress, infections or pregnancy. These acute forms satisfy all the criteria of severe disease, but last only for a few months.

The question we asked here was whether COP could be associated with a higher risk of cardiovascular and metabolic comorbidities, independently of severity, in adulthood. Because of the study design (i.e. a cross-sectional study on adults with active psoriasis), transient psoriasis in childhood, like napkin psoriasis or guttate psoriasis, was excluded from the study. We included all patients with psoriasis, regardless of their disease severity, and considered as severe in the multivariate analysis only those receiving systemic treatment or a biologic on the day of inclusion. Probably because patients consulted dedicated psoriasis centres mostly in hospitals, two-thirds of the patients met the criteria for severe psoriasis. In any case, neither age at onset nor disease duration was associated with the frequency of cardiovascular and metabolic comorbidities in adulthood.

The psoriatic march tries to explain the potential link between psoriasis and, more generally, chronic inflammatory diseases, like Crohn disease and rheumatoid arthritis, and the high frequencies of cardiovascular events associated with these entities. Systemic inflammation can cause insulin resistance, which, in turn, induces endothelial cell dysfunction, leading

to atherosclerosis and, eventually, to myocardial infarction or stroke.[12] Therefore we hypothesized that COP might be associated with higher rates of cardiovascular and metabolic diseases; this hypothesis was not substantiated. Univariate analysis results suggested that COP protected against comorbidities, except for tobacco use, but COP patients were younger than those with AOP, and it is well known that the frequencies of diabetes, dyslipidaemia, hypertension, obesity, abdominal obesity and MACE increase with age. On the other hand, smoking decreased with age. According to our multivariate analysis, age was always significantly associated with higher percentages of all those risk factors. Sex was mainly linked to frequencies of hypertension and smoking, and the severity of psoriasis to obesity. A recent Taiwanese case–control study evaluated whether the sequence of events psoriasis and metabolic disorder onsets could affect the risk for subsequent development of cardiovascular complications.[39] Psoriasis was considered the initiator of the inflammatory march when comorbidities developed after its onset, and was a potent amplifier of pre-existing comorbidities. If psoriasis served as the initiator of inflammation, the risk of developing cardiovascular disease was lower than when it served as the amplifier of disease. Future studies should collect data on such chronological events for multivariate analyses to evaluate the true impact of age at onset.

The results of this study showed that childhood onset of psoriasis was not associated with the frequency of cardiovascular and metabolic comorbidities in adulthood, and our multivariate analysis retained the higher frequency of obesity as being significantly associated with the severity of psoriasis and psoriatic arthritis.

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ORIGINAL ARTICLE

Evaluation of risk factors for body weight increment in psoriatic patients on infliximab: a multicentre, cross-sectional study

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Abstract

Background A significant weight gain has been reported in patients with psoriasis treated with anti-tumour necrosis factor-alpha agents. Among these patients, there are contradictory results about risk factors for weight gain.

Objective Assessing risk factors for weight increment in psoriatic patients on infliximab (IFX).

Methods This study was a 4-month, non-interventional, cross-sectional, multicentre study on adults with psoriasis performed in 19 French dermatological centres. All the patients who received IFX for at least 1 year were prospectively included, with retrospective analysis of data. Impact of sex, age, severity of the disease, cardiovascular and metabolic comorbidities, and previous and simultaneous systemic treatments on weight changes, was analysed. Weight gain was defined as an increment of more than 2% of baseline weight.

Results Overall, 191 psoriatic patients (males: 68.6%; mean age: 46.9 years) were included. Mean weight gain was 1.6 kg (2.1%) after 1 year of IFX. Half (48.2%) suffered from a weight gain, and 9.9% from a weight increment of 10% or more. Baseline weight and Body Mass Index, and cardiovascular and metabolic comorbidities did not influence weight. Men ($P = 0.007$) and patients with severe psoriasis (BSA, $P = 0.005$) had a tendency to put on weight. Patients with a hospital dietary follow-up ($P = 0.01$; OR = 0.36 [0.16–0.79]) and patients on methotrexate ($P = 0.03$; OR = 0.41 [0.18–0.93]) during IFX treatment are thinner, in a multivariate analysis.

Conclusion Severe weight increment is frequent on IFX treatment, mainly in men, and patients with severe psoriasis. Dietary follow-up or simultaneous use of methotrexate could limit this weight increment.

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Conflicts of interests

E. Mahé is a consultant for Janssen-Cilag; has received research support by MSD; and has received speaker honoraria from Abbott, Janssen-Cilag, Pfizer, and Schering-Plough.

Z. Reguiai is a consultant for Janssen-Cilag and Pfizer; has been an investigator for Abbott, Novartis, and Pfizer; has

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C. Girard has received speaker honoraria from Abbott, Janssen-Cilag and Leo.
E. Estève has received speaker honoraria from Abbott, Janssen-Cilag, Leo, Pfizer and Schering-Plough.
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J.-L. Schmutz has been an investigator for Pfizer.
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P. Bravard has been an investigator for Abbott; and has received speaker honoraria from Abbott, Janssen-Cilag, Pfizer and Schering-Plough.
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Psoriasis is a lifelong and chronic T-cell mediated disease of the skin and occasionally the joints which affects up to 3% of the population worldwide.[1] An increasing number of epidemiological studies have linked metabolic syndrome and its components – that is, obesity, dyslipidemia, hypertension, diabetes – with immune-mediated conditions, such as psoriasis and rheumatoid arthritis.[2–6]

Given that tumour necrosis factor-alpha (TNF-α) plays a key role in the pathogenesis of various inflammatory conditions, several biological treatment – that is, adalimumab (Humira®; Abbott France, Rungis, France), etanercept (Enbrel®; Pfizer, Paris, France) and infliximab (Remicade®; MSD France, Courbevoie, France), the three drugs licensed for the treatment of patients with moderate-to-severe plaque psoriasis and psoriatic arthritis – have been developed to specifically inhibit its function. Although these three anti-TNF-α are effective in psoriasis, presently little is known about their effects on metabolic syndrome components in these patients.[7]

Recent studies have shown that long-term use of anti-TNF-α is associated with a weight gain in patients with psoriasis,[8–13] Crohn's disease,[14] and rheumatological diseases including psoriatic arthritis,[9–11,15,16] spondylarthropathy[15,16] and rheumatoid arthritis.[17,18] Little is known about risk factors for weight gain among these patients. Some studies have identified correlation with inflammatory syndrome[15,16], or baseline body weight and weight gain.[12,13,16]

In this cross-sectional multicentre study, we evaluated risk factors for weight changes in psoriatic patients on anti-TNF-α. In France, infliximab (IFX) is the only anti-TNF-α that requires hospital follow-up because of bimonthly intravenous infusions. We chose to study only patients on IFX, to make sure of the quality of information on weight follow-up.

Methods

A non-interventional, cross-sectional, multicentre study on adults with psoriasis was performed in 19 dermatological centres in France from April to July 2012. The dermatological centres are members of the *Groupe d'Etude Multicentrique* Resopso (http://resopso.fr), a French association of dermatologists who get a great interest in developing networking activities in the field of psoriasis. These 19 centres are university (n = 5), general (n = 12), and military hospitals (n = 2).

Patients were consecutively included if: (i) they were 18-years old or more; (ii) they had psoriasis (skin and/or joint involvement), diagnosed according to clinical criteria; (iii) they were on IFX for 1 year, without any disruption; and (iv) they had been

weighed at the start of the treatment and 1 year later (± 1 month).

Patient evaluation

The one-page case report form included 24 items on (i) patients: age, sex; (ii) psoriasis: clinical aspects, inflammatory arthritis, history of systemic treatments before and during IFX therapy, severity of the disease assessed by Psoriasis Area and Severity Index (PASI), body surface area (BSA) involved, and the Dermatology Life Quality Index (DLQI); (iii) cardiovascular risk factors: hypertension, current smoking; (iv) metabolic diseases: weight (baseline, and after 6 and 12 months of IFX treatment), Body Mass Index (BMI), diabetes, and dyslipidemia; (v) IFX treatment and events during the treatment: dosage after 1 year, dietary follow-up at hospital (consultation with a dietician), and sporting activity (at least 1 h per week of sport activity, all year long, without disruption) during the year of treatment. Dosage of IFX was initially 5 mg/kg at week 0, 2, 6 and then every 8 weeks by intravenous infusion. Dosage could be modified according to clinical efficiency.

Body Mass Index was calculated as weight in kilograms divided by height in metres squared. Underweight was defined by a BMI < 18.5 kg/m^2, normal weight by a BMI ≥ 18.5 and < 25 kg/m^2, overweight by a BMI ≥ 25 and < 30 kg/m^2, and obesity by a BMI ≥ 30 kg/m^2.[19]

Diabetes mellitus was diagnosed if patients had a fasting plasma glucose level of 7 mmol/L (1.26 mg/L) or higher, or reported the use of oral glucose-lowering medication or insulin. Participants were classified as having hypertension if they had a systolic blood pressure of 140 mm Hg or higher or a diastolic blood pressure of 90 mm Hg or higher, or if they reported the use of blood pressure-lowering medication. Dyslipidemia was defined by low-density lipoprotein (LDL) cholesterol levels of 160 mg/dL (4.14 mmol/L) or higher, high-density lipoprotein (HDL) cholesterol levels of less than 40 mg/dL (1.03 mmol/L) and triglyceride levels of 200 mg/dL (2.26 mmol/L) or higher. Patients who were taking lipid lowering medication were also classified as dyslipidemic. Current smoking was defined by a consumption of at least five cigarettes per day for at least 1 year.

There is no definition of what 'stable' weight is at 1 year. So, we suggested to define 'stable' weight as a change of less than ± 2% of baseline weight – for example, ± 1 kg for a 50 kg patient, and ± 2 kg for a 100 kg patient.

Statistics

Quantitative data were expressed as mean ± standard deviation (SD) and range, qualitative data as frequency and percentage. Comparisons of means were performed using ANOVA. Comparisons of frequencies were performed using the Chi-squared test.

An ordinal logistic regression was used to determine the predictors of weight gain. A P-value < 0.05 was considered statistically significant. Statistical analyses were performed using SAS software v 9.3 (SAS Institute Inc, Cary, NC, USA).

Results

Of the 208 patients seen in the 19 centres during the 4-month study, 17 were not included because, at least one weight was missing ($n = 15$), or they were duplicated ($n = 2$). So, 191 patients on IFX, during 1 year without disruption, have been evaluated.

Baseline characteristics of the patients

The mean age of patients was 46.9. Two-thirds (68.6%) were males. Mean duration of the disease was 19.8 ± 13.2 years (ranges: 1–64 years). Mean baseline weight and BMI were 84.2 ± 20.4 kg, and 28.7 ± 6.4 kg/m^2 respectively. Overweight (40.1%) or obesity (26.9%) was found in 67.0% of patients; 10.5%, 27.4%, 27.4% and 31.4% of patients suffered from diabetes, dyslipidemia, hypertension and active smoking at baseline respectively (Table 1).

Sixty-two patients had significant chronic comorbidities: psychiatric symptoms (depression, $n = 19$; psychotic syndrome, $n = 4$); alcoholism ($n = 14$), drug addiction, $n = 4$, liver (HCV infection, $n = 2$; cirrhosis, $n = 3$; unexplained chronic hepatitis, $n = 2$; CBP, $n = 2$), skin (bullous pemphigoid, $n = 2$; systemic sclerosis, $n = 1$; hidradenitis suppurativa, $n = 1$), thyroid (hypothyroidism, $n = 5$; hyperthyroidism, $n = 1$), digestive (Crohn's disease, $n = 1$; haemorrhagic rectocolitis, $n = 1$, coeliac disease, $n = 1$) or lung diseases (asthma, $n = 5$; chronic respiratory insufficiency, $n = 4$).

Characteristics of psoriasis

The predominant type of psoriasis was plaque psoriasis in 82.7% of patients, and 40.3% of patients had joint involvement. Mean PASI, BSA and DLQI at the start of IFX were 22.4/72, 40.7% and 15.5/30 respectively (Table 1).

Among traditional systemic treatments, methotrexate had been previously used by 145 (75.9%) patients, acitretine by 94 (49.2%), cyclosporine by 84 (44.0%), etretinate by 16 (8.4%), leflunomide by 3 (1.6%) and mycophenolate mofetil or azathioprine by 1 (0.5%). Among biological systemic treatments, etanercept had been previously used by 50 (26.2%) patients, adalimumab by 29 (15.2%), efalizumab by 39 (20.4%), ustekinumab by 4 (2.1%) and tocilizumab by 1 (0.5%). Five (2.6%) patients had previously received IFX. Sixty-three (33.0%) had been previously treated with one biological, 18 (9.4%) with two, 7 (3.7%) with three and 2 (1.0%) with four (Table 1). Among the 191 patients, 5 (2.6%) were naive of traditional or biological systemic treatment before IFX.

The most frequent general treatments used during the 3 months before starting IFX were methotrexate (31.3%), cyclosporine (22.1%) or another anti-TNF-α (19.6%). Fourteen (7.1%) patients had no general treatment during the 3 months before starting IFX.

Events during the IFX 1-year treatment

During the 1-year treatment, 34 (17.8%) patients had another general systemic treatment, mainly methotrexate ($n = 32$, 16.8%) (Table 1). Only one (0.5%) patient was included in a therapeutic study.

Table 1 Clinical data of the 191 psoriatic patients on infliximab, and risk factors for weight change

	All the patients *n* = 191	Weight changes			*P*-value
		Thinner *n* = 41	Stable *n* = 58	Increment *n* = 92	
Sex ratio (male/female)	2.18	0.95	3.5	2.5	0.007
Age, years (mean ± SD)	46.9 ± 12.7	48.8 ± 13.1	46.0 ± 12.6	46.6 ± 12.7	NS
Duration of the disease, years (mean ± SD)	19.8 ± 13.2	21.8 ± 11.9	21.7 ± 13.8	17.7 ± 13.2	NS
Comorbidities at baseline					
Weight (kg), mean ± SD	84.2 ± 20.4	86.6 ± 23.1	83.4 ± 22.5	83.6 ± 17.7	NS
BMI (kg/m^2), mean ± SD	28.7 ± 6.4	30.5 ± 7.6	27.7 ± 6.1	28.5 ± 5.8	NS
BMI classes					
Underweight, *n* (%)	7 (3.9)	1 (2.5)	4 (7.5)	2 (2.3)	NS
Normal weight	48 (26.8)	11 (27.5)	15 (28.3)	22 (25.6)	–
Overweight, *n* (%)	57 (31.8)	9 (22.5)	16 (30.2)	32 (37.2)	–
Obesity, *n* (%)	67 (37.4)	19 (47.5)	18 (34.0)	30 (34.9)	–
Diabetes, *n* (%)	20 (10.5)	3 (7.5)	4 (6.9)	13 (14.1)	NS
Dyslipidemia, *n* (%)	52 (27.4)	13 (32.5)	13 (22.4)	26 (28.3)	NS
Hypertension, *n* (%)	52 (27.4)	14 (35.0)	10 (17.2)	28 (30.4)	NS
Smoking, *n* (%)	58 (31.4)	13 (33.3)	21 (37.5)	24 (26.7)	NS
Severity of psoriasis at baseline					
PASI,/72 (mean ± SD)*	22.4 ± 13.1	19.7 ± 11.3	21.5 ± 15.0	24.4 ± 12.3	NS
BSA, % (mean ± SD)*	40.7 ± 24.5	30.3 ± 22.3	37.2 ± 13.2	47.2 ± 24.5	0.005
DLQI,/30 (mean ± SD)*	15.5 ± 6.4	17.9 ± 7.1	12.8 ± 4.9	16.3 ± 6.5	NS
Joint involvement, *n* (%)	77 (40.3)	23 (56.1)	17 (29.3)	37 (40.2)	0.02
Dosage of IFX at the end of the 1-year treatment, *n* (%)†					
Same dosage (5 mg/kg/8 weeks)	156 (81.7)	34 (82.9)	48 (82.8)	74 (80.4)	NS
Lower dosage (< 5 mg/kg/8 weeks)	7 (3.7)	1 (2.4)	1 (1.7)	5 (5.4)	–
Higher dosage(> 5 mg/kg/8 weeks)	28 (14.7)	6 (14.6)	9 (15.5)	13 (14.1)	–
General treatment during the 3 months before initiation of IFX, *n*(%)					
Traditional systemic therapies					
Acitretin	8 (4.9)	2 (6.5)	1 (2.0)	5 (6.0)	NS‡
Cyclosporine	36 (22.1)	6 (19.4)	11 (22.4)	19 (22.6)	NS‡
Methotrexate	51 (31.3)	12 (38.7)	14 (28.6)	25 (30.1)	NS‡
Biological systemic therapies					
Adalimumab	14 (8.6)	2 (6.5)	7 (14.3)	5 (6.0)	NS‡
Etanercept	18 (11.0)	7 (22.6)	3 (6.1)	8 (9.6)	NS‡
Efalizumab	17 (10.4)	0 (0)	8 (16.3)	9 (10.8)	NS‡
No treatment	14 (8.6)	2 (6.5)	4 (8.2)	8 (9.6)	NS‡
General treatment during the 1-year treatment with IFX, *n*(%)					
Acitretin	2 (1.0)	0 (0)	1 (1.7)	1 (1.1)	NS
Methotrexate	32 (16.8)	12 (29.3)	9 (15.5)	11 (12.0)	0.049§
Dietary management	39 (22.7)	14 (37.8)	12 (23.1)	13 (15.7)	0.03
Sport activity	15 (8.7)	4 (10.8)	5 (9.4)	26 (7.2)	NS

*Evaluation of PASI, BSA and DLQI was available in 96, 135 and 110 patients respectively.
†Lower dosage: 5 mg/kg/10 weeks; higher dosage: either dosage was increased or inter-dose time was decreased.
‡Comparing the patient with the treatment used during the 3 months before initiation of IFX vs. all other patients.
§Comparing patients receiving methotrexate vs. patients without systemic treatment associated to IFX.
BMI, Body Mass Index; BSA, body surface area; DLQI, Dermatology Life Quality Index; IFX, infliximab; NS, not statistically significant; PASI, Psoriasis Area and Severity Index.

Dosage of IFX after 1 year of treatment was unchanged (5 mg/kg/8 weeks) for 156 (81.7%) patients, was lower for 7 (3.7%; 5 mg/kg/10 weeks, $n = 7$), and higher for 28 (14.7%; 10 mg/kg/8 weeks, $n = 1$; 10 mg/kg/6 weeks, $n = 1$; 7.5 mg/kg/6 weeks, $n = 2$; 5 mg/kg/7 weeks, $n = 7$; 5 mg/kg/6 weeks, $n = 17$).

No severe clinical events were reported during the 1-year treatment. During the treatment, 39 (22.7%) patients had a dietary

follow-up, either dietetic consultations or diet, carried out at the hospital. Fifteen (8.7%) had sporting activities: jogging, $n = 5$; body building, $n = 3$; cycling, $n = 2$; and football, $n = 1$ (lacking data, $n = 4$).

Effects of IFX treatment on body weight

The mean weight gain after 6 months of IFX was 0.6 kg (+ 1.0%), and, after 1 year, 1.6 kg (+ 2.1%) (Table 2). Among the 191 patients, about one quarter was either thinner (21.5%) or stable (30.4%) after 1 year of IFX, and half (48.2%) had a weight increment. Among the patients who had put on weight, the mean weight change was 7.8%. Nineteen (9.9%) of them had a weight gain of more than 10% (Fig. 1). If 26.9% of patients were obese at the start of the treatment, they were 30.7% after 1 year.

Risk factors for body weight changes (univariate analysis)

Men were more likely to put on weight than women ($P = 0.007$) after 1 year of treatment. One-year change of body weight was not correlated with the age of the patient, baseline body weight, BMI, class of BMI, cardiovascular comorbidities – that is, hypertension, smoking – or metabolic comorbidities – that is, diabetes, dyslipidemia – (Table 1). None of the other comorbidities (hypothyroidism, alcoholism, etc.) was associated to body weight changes.

There was a tendency to put on weight if psoriasis was clinically more severe (PASI: non-significant; BSA: $P = 0.005$). Fewer patients with joint involvement had a 'less stable' weight either it decreased or increased ($P = 0.02$) (Table 1).

None of the systemic treatments administered just before IFX was correlated with weight changes. When methotrexate was associated with IFX, there was a significant tendency to become thinner ($P = 0.049$). IFX dosage alterations were not associated with weight changes (Table 1).

A dietary follow-up in hospital was associated with thinning ($P = 0.03$). Sporting activities did not alter final weight.

If we compare patients with a very high decrease in weight (> −10%, $n = 9$) to patients with a very high increment in weight (> +10%, $n = 19$), gender (male: 2/9 in 'the decreased group' vs. 14/19 in 'the incremented group', $P = 0.03$) was correlated with weight increment. Baseline weight (96.6 ± 20.1 kg in the thinned group vs. 76.8 ± 12.5 kg in the incremented group, $P = 0.001$) and BMI (34.5 ± 7.8 kg/m^2 in the thinned group vs. 27.9 ± 6.5 kg/m^2 in the incremented group, $P = 0.03$) were correlated with weight increment. No correlation was identified for other parameters (data not shown).

Risk factors for body weight changes (multivariate analysis)

The predictor variables included in the multivariate analysis were sex, baseline BMI, dietary follow-up and simultaneous use of methotrexate. Severity of the disease (BSA) was not included in this analysis because of the high number of missing data (29%). Sex ($P = 0.19$) and baseline BMI ($P = 0.85$) have no influence on weight variation in the multivariate analysis. Dietary management ($P = 0.01$; OR = 0.36 [0.16–0.79]) during IFX treatment and simultaneous methotrexate intake ($P = 0.03$; OR = 0.41 [0.18–0.93]) may provide protection against weight gain.

Table 2 Body weight and BMI changes after 1 year of IFX treatment

	Duration of IFX	
	6 months	1 year
Weight, mean ± SD [ranges: min–max]		
kg	0.6 ± 5.8 [−24–+20]	1.6 ± 7.3 [−42–+35]
%	1.0 ± 7.0 [−28.6–+31.7]	2.1 ± 8.5 [−45.7–+37.3]
BMI, mean ± SD [ranges: min–max]		
kg/m^2	0.1 ± 2.0 [−7.9–+6.0]	0.5 ± 2.6 [−14.2–+13.8]
%	0.9 ± 7.0 [−28.6–+31.7]	1.9 ± 8.6 [−45.7–+37.3]

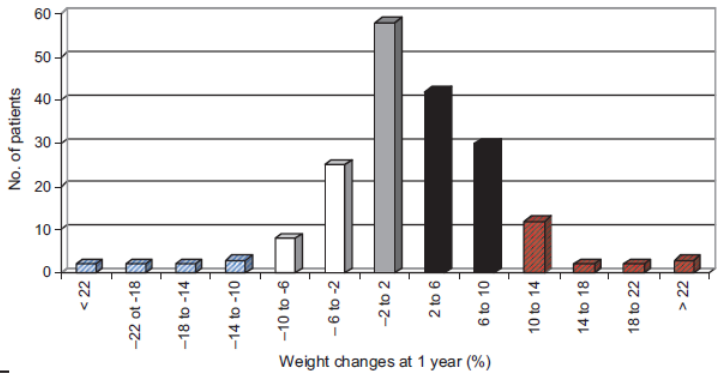

Figure 1 Weight changes after 1 year of IFX. Percentage of variation of weight between initiation of treatment and after 1 year of IFX [white: thinner; grey: stable weight; black: weight gain; red: high weight increment (> +10%); in blue: high weight decrease (> −10%)].

Discussion

This multicentre cross-sectional study evaluated risk factors for weight change, in real life conditions, in 191 psoriatic patients on IFX. First, this study confirms that IFX can induce weight gain in half of the patients, and 10% of them have an increment of more than 10% of their baseline weight after 1 year of treatment. Men and patients with severe psoriasis are at higher risk for weight gain, while simultaneous methotrexate use and hospital dietary follow-up have a positive effect on weight.

Tumour necrosis factor-alpha is deeply involved in body weight homeostasis. Research suggests that the effects of TNF-α on lipid metabolism mainly display five features: (i) it suppresses free fatty acid uptake and promotes lipogenesis; (ii) it induces lipolysis; (iii) it inhibits lipid metabolism-related enzyme activity; (iv) it regulates cholesterol metabolism; (v) it regulates other adipocyte-derived adipokines. The molecular mechanisms underlying these actions are complex and several signal transduction pathways might be involved.[20,21] So, inhibiting TNF-α activity can alter lipid metabolism and can explain weight variations.

To our knowledge, 12 published studies (including ours) show that long-time use of anti-TNF-α induces weight increment (Table 3). In psoriasis, it has been linked to IFX,[8,9,11–13] etanercept[8–11] and adalimumab.[9] In all these studies, the mean body weight gain remains very low, from 0.6 to 2.6 kg after 1 year of treatment. That could be considered 'stable weight' or physiological increment of weight if we consider that (i) even if we use the same scale during a 1-year study, we cannot exclude tare variations; (ii) weight is a dynamic parameter during the day, and from week to week, dependent of diet or hydration for example; (iii) the prevalence of obesity increases from year to year independently of any disease or treatment. As an example, between 2006 and 2009 in the French general population, the prevalence of obesity increased from 13.1% to 14.5% (+10.7%);[22] (iv) the prevalence of obesity increases with age. In recent French data, the prevalence of obesity has been shown to increase progressively from 14.9% in 35–45 year-old people to 21.2% in 55–64 year-old people.[22] (v) patients with very severe disease, or low baseline weight, have a tendency to have a higher weight increment.[12,15,16] Very severe diseases are associated with syntheses of cytokines including TNF-α. These pro-inflammatory cytokines are important mediators of cachexia.[7,14,18,23] It could be hypothesized that very active treatment could help to make up for 'true baseline weight'. (vi) and finally in all the studies evaluating weight increment due to anti-TNF-α, weight increment is gradual and progressive, and increases slowly from month to month, or year to year, without a 'peak' (Table 3) and could reflect spontaneous weight gain according to ageing and evolution of the population, and correction of cachexia.

Nevertheless, weight increment in psoriatic patients on anti-TNF-α seems to be a real problem for some patients. First, in our study we decided to isolate patients with 'stable' weight (variation of ± 2%: one-third of patients). Outside this group, 'significant' weight gain was found in half of our psoriatic patients. We also identified a little group of patients who had a very important weight increment (10% of patients: a more than 10% weight increment). Among patients receiving anti-TNF-α, a major weight gain has been reported in previous studies in children and adults, with skin or rheumatological diseases, leading to a discontinuation of treatment due to weight gain in some of them.[9,17,24] Saraceno has shown that among patients with weight gain, 31.8% of patients on etanercept and 25.0% on adalimumab had an increase in weight of more than 10% in a 48-week evaluation.[9] Alcorn has shown that 15% of rheumatoid arthritis patients on anti-TNF-α gained 6 more kg in the first year of therapy.[17] Another clinical argument in favour of the direct role of anti-TNF-α in weight increment is the data from controlled studies comparing TNF-α antagonists to methotrexate or 'non-biological' systemic therapies.[8,9,12,13] In all these studies, while a weight increment was observed in patients on anti-TNF-α, methotrexate was always associated with a stable weight or a weight decrease. Identification of the population with a higher risk for a very high weight increment – that is, male gender, patients with severe psoriasis and low baseline weight or BMI – is another argument in favour of the specific influence of these treatments on weight.[12,13,15,16]

Previous studies have identified risk factors for weight gain (Table 3): severe inflammatory syndrome in spondylarthropathic patients,[15,16] or either low[12] or high baseline weight.[13] Other studies have not identified risk factors.[8,9,18] All these studies were monocentric, sometimes involving two or three anti-TNF-α blends, some excluded patients on diets, patients with diabetes or 'severe comorbidities'.[9,17] So to reduce the centre- and drug-effects, we performed a multicentre study only with patients on IFX. First, our study found that clinical severity of the disease was associated with a higher risk of weight increment. Briot also found that severe inflammation, defined by high C reactive protein and erythrocyte sedimentation rate in spondylarthropathy was correlated with weight gain.[15,16] We know that inflammation is closely linked to TNF-α activity and lipid metabolism.[25,26] Low baseline weight is correlated with a high weight gain, as previously reported[12,16] and gender (herein, higher risk of weight gain for males). It has been shown that lipid metabolism and TNF-α sensibility differ according to weight (obese vs. normal weight patients)[27] or gender.[28] The complex links between TNF-α and these parameters can explain why some groups of patients are more sensitive to weight changes on anti-TNF-α.

The positive effect of simultaneous use of methotrexate on weight gain is interesting. It has been shown that methotrexate could reduce the risk of cardiovascular disease and atherosclerosis, particularly at lower doses, in patients with chronic inflammatory disorders or even in patients with persistent inflammatory responses.[6,29] In studies evaluating psoriatic patients that compared the effect of anti-TNF-α and methotrexate on weight, methotrexate was never associated with significant weight alterations.[8,9,13] A study has evaluated the effects of

Table 3 Anti-TNF-α and body weight changes. Data from the literature

No.	Study	Study design	Disease	Treatment (No. patients)	Delay	Weight change, kg(%)	BMI change, kg/m^2 (%)	Risk factors for weight change
1	Franchimont, 2005[14]	Prospective	Crohn's disease	IFX (20)	4 weeks	0.8		
2	Briot, 2005[15]	Prospective	Spondylarthropathy (21.1% psoriasis)	IFX (17) and ETC. (2)	6 months/1 year	1.8 (2.6)/2.2 (3.4)		No difference according to gender, baseline body weight, use of corticosteroids and methotrexate. Positive correlation with baseline CRP and ESR
3	Marcora, 2006[18]	Prospective	Rheumatoid arthritis	ETC. (12) MTX (12)	24 weeks	0.9 0.9		
4	Gisondi, 2007[8]	Retrospective	Psoriasis	IFX (40) ETC. (58) MTX (43)	6 months	2.5 1.5 − 0.6	0.8 0.5 − 0.2	No difference according to age, gender, BMI classes and psoriasis severity
5	Briot, 2008[16]	Prospective	Spondylarthropathy (6.6% psoriasis)	IFX (55) and ETC. (47)	1 year/2 years 2 years	2.2/2.2		No difference according to use of corticosteroids and methotrexate. Positive correlation with baseline body weight, CRP and ESR
6	Saraceno, 2008*[9]	Retrospective	Psoriasis (37.8% arthritis)	IFX (50) ETC. (50) ADA (30) MTX (50)	12 weeks /24 weeks /48 weeks	0.2/1.1/1.5 0.5/1.7/2.2 1.6/2.5/2.6 0.1/0.2/0.2	0.1/0.4/0.5 0.2/0.6/0.7 0.5/0.8/0.9 −0.1/0.0/0.0	No difference according to gender, plaque psoriasis vs. arthritis ETC.: weight increase higher in lean individuals
7	Esposito, 2009[10]	Retrospective	Psoriasis	ETC. (100)	12 weeks/ 24 weeks	1.8/3.1	0.7/1.1	
8	Alcorn, 2010[17]	Retrospective	Rheumatoid arthritis	Anti-TNF-α (53)	1 year	4.2 (73% of patients)		No difference according to age, baseline body weight
9	Di Renzo, 2011[11]	Prospective	Psoriasis (20) Psoriatic arthritis (20)	IFX (28) and ETC. (12)	24 weeks	2.2 (2.6) 1.6 (2.1)	0.7 (3.8) 0.5 (3.7)	
10	Florin, 2012[12]	Retrospective	Psoriasis	IFX (35) Non-biological therapies (16)	1 year/3 years	3 (3.6)/10.5 (6.0) −2.0 (1.2)/	1 −0.7	Weight gain is more important if BMI < 25 kg/m^2
11	Forien, 2012[13]	Retrospective	Psoriasis	IFX (18) MTX (25)	1 year	0.6 −2.2		Positive correlation with baseline weight
12	Mahé, 2012	Retrospective	Psoriasis	IFX (191)	6 months/1 year	0.6 (1.0)/1.6 (2.1)		

Studies 2 and 5 are from the same group, and 6, 7 and 9 from another group. There is no information in the studies if patients were included in two or three publications.

*A group with efalizumab was evaluated, but not included in the table since this drug is not longer licensed.

ACT, acitretine; ADA, adalimumab; BMI, Body Mass Index; CRP, C reactive protein; CyA, cyclosporine; ESR, erythrocyte sedimentation rate; ETC., etanercept; IFX, infliximab; MTX, methotrexate.

long-term etanercept treatment on growth in children with juvenile idiopathic arthritis, the results contradicting ours.[30] The authors have shown statistically significant increases from baseline in the mean BMI percentiles in etanercept groups (etanercept alone, and etanercept with methotrexate) compared with the methotrexate group. However, there were no difference between the etanercept group alone vs. the etanercept plus methotrexate one. We also know that methotrexate interacts with the lipid metabolism of endothelial cells and reduce atherogenesis. Despite its anti-atherogenic potential *in vitro* and *in vivo*, little remains known about the impact of clinical use of low-dose MTX on lipid metabolism in humans.[31,32] Therefore, the exact role of methotrexate in weight variations is not clear and should be confirmed in larger studies.

Finally, educational strategies during treatment with IFX such appropriate diet regimen and physical activity to reduce this 'side-effect' associated with the treatment seem. In our study, as in Florin's study,[12] it has been suggested that hospital dietary follow-up is associated to a reduction of weight gain. We did not shown impact of sport activity on weight but low frequency of sport activity in our population could be an explanation for this absence of statistical difference. So, we can propose that educational strategy – that is, hospital dietary follow-up and physical activity – should be systematically propose when we start IFX, and probably other anti-TNF-α.

Conclusion

Severe weight increment is frequent on IFX treatment, mainly in men, and patients with severe psoriasis. Dietary follow-up or simultaneous use of methotrexate could limit this weight increment. It is time-dependent and not dose-dependent. Weight must be monitored in psoriatic patients on anti-TNF-α since a significant proportion of psoriatic patients suffers from other comorbidities such as cardiac diseases, diabetes, dyslipidemia or hypertension. Early monitoring of weight variation could also facilitate early diet counselling and regular nutritional visits.

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Severe androgenetic alopecia as a proxy of metabolic syndrome in male psoriatic patients older than 59 years

Background: Whereas several studies have underlined the association between severe psoriasis and metabolic syndrome (MetS), the association of androgenetic alopecia (AGA) and MetS have yielded inconsistent results. *Objective:* To investigate the relationship between AGA and the components of MetS in a population of psoriatic male patients. *Methods:* A non-interventional, cross-sectional, multicenter study was conducted in France. A standardized questionnaire was completed, including information on components of MetS and other possible risk factors. MetS was defined in this study as a combination of three or more of the four components of MetS: waist circumference, hyperlipidemia, diabetes mellitus and hypertension. In addition, a standardized simplified Norwood classification limited into 5 grades (0-4) was used. *Results:* In a total of 1073 male patients, hypertension, high waist circumference, diabetes mellitus and hyperlipidemia were observed in 28%, 59%, 11%, and 31%, respectively. In age-adjusted multivariate analysis, severe AGA (grade 3-4 *versus* grade 0) was associated with the presence of at least one component of MetS. By groups of age, a statistically significant association of severe AGA and MetS was demonstrated in patients over 59 years. Severe AGA was also associated with a first degree familial history of major cardiovascular event in patients older than 59 years. *Conclusions:* Our study, based on a simplified but stringent definition of MetS, confirmed the link between severe AGA and individual components of MetS in psoriatic patients. This argues for careful follow-up with regular screening in male psoriatic patients with severe AGA in order to early detect determinants of MetS.

Key words: psoriasis, metabolic syndrome, androgenetic alopecia, hypertension

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Psoriasis is a chronic inflammatory skin disease that affects approximately 2-3% of the population in western countries [1, 2]. Patients with psoriasis appear to be at higher risk for metabolic syndrome (MetS) and severe cardiovascular events. The National Psoriasis Foundation proposed in 2008 screening guidelines and recommendations for the management of cardiovascular risk factors in psoriatic patients, although the latter is still to be routinely conducted [3]. The association of androgenetic alopecia (AGA) with hypertension, abnormal serum lipid

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profiles, obesity, and insulin resistance has been suspected since the early nineties and AGA is now considered as a marker of the MetS in the general population [4, 5].
In this context, we thought to prospectively evaluate the association between AGA severity and components of the MetS in psoriatic male patients.

Methods

This was a prospective, non-interventional, cross-sectional, multicenter study. It was an ancillary study of another study [6]. Consecutive male psoriatic patients aged 18 years old or older were recruited from 29 French dermatological centres between June 15th and October 31st 2011. All dermatologists involved in the study were participants of the Groupe d'Etude Multicentrique Resopso (http://resopso.fr), a French association of dermatologists with a great interest in developing networking activities in the field of psoriasis. For each patient, a standardized questionnaire specially designed for the study was completed by the referent dermatologists. This questionnaire included demographic and clinical data, including affected body surface area (<10%, 10 to 20%, >20%), scalp involvement (yes/no), psoriatic arthritis (yes/no). In addition, components of MetS (presence or absence of diabetes mellitus type 2, dyslipidemia, hypertension, waist circumference > 94 cm), history of cardiovascular event, first degree of familial history of severe androgenic alopecia (father), score of AGA, and ongoing treatment for psoriasis (systemic, biologic) were also retrieved. The diagnosis of AGA was made by the referent dermatologist using the standardized simplified Norwood classification with the aid of a figure. Scores of AGA were limited into 5 categories: 0 to 4 [7]. Stages 1, 2, 3, and 4 were bitemporal recession, frontoparietal recession with vertex thinning, vertex loss with bridge of hair over the midscalp and extensive baldness, respectively.
The definition of MetS was based on the combination of three or more of the four following criteria: (i) waist circumference >94 cm; (ii) hypertension defined by arterial pressure ≥130/85 mmH, or treatment for hypertension; (iii) abnormal lipid serum values, or treatment for hyperlipemia; and (iv) diabetes mellitus, or treatment for diabetes mellitus. Current smoking habits were also noted.
Quantitative data were expressed as mean ± standard deviation; qualitative data as frequency and percent. Comparisons of means were performed using the Student's t-test and Analysis of Variance. Comparisons of frequencies were performed using the Chi square test and the Fisher's exact test, as appropriate.
A logistic regression was used to asses the relationship between risk factors and AGA, adjusted on age. A p value <0.05 was considered statistically significant. Statistical analysis was performed using SAS software version 9.3 (SAS Institute Inc, Cary, NC, USA). Analysis was done for the total population and by groups of age: 18-29, 30-39, 40-49, 50-59 and older. Further, we compared patients with AGA grade 0 *versus* those with moderate and severe AGA (type 3 and 4) for all clinical parameters, including familial history and cardiovascular events, severity of psoriasis (percentage of body surface area involved) and scalp psoriasis.The study was approved by our local ethic committee and the database was declared to the CNIL (Commission Nationale de l'Informatique et des libertés) Declaration N° 1519010.

Results

Description of the psoriatic population

A total of 1073 patients were enrolled in the study. Characteristics of the studied population are described in *table 1*. Of the total population, 71.6% of the patients had moderate to severe psoriasis with the assumption that psoriasis with a body surface area over 10% may be considered as moderate to severe.
The characteristics of the population were: mean age 48.7 ± 14.4 years, 58% were treated with systemic treatments, 22% were on biologics. These patients were mainly treated for moderate to severe psoriasis: their maximal body surface areas were <10%, 10-20%, and >20%, in 273, 281, and 488 patients, respectively.
Diabetes mellitus, abnormal serum lipid profiles, hypertension, and high waist circumference were observed in 11%, 31%, 28%, and 59%, respectively *(table 1)*. Mean body weight was 83.8 ± 16.5 kg, mean height 175 ± 7.1 cm, and mean waist circumference was 99 ± 14.9 cm. Of the patients 38.9% had familial history of AGA.

Table 1. General characteristics and pathological conditions in the 1,073 male psoriatic patients according to the severity score of AGA

	Patients	AGA					p*
		0	1	2	3	4	
Number of patients	1,073	397	138	225	159	154	
Age (y), mean ± SD	48.7 ± 14.4	43.6 ± 14.2	46.2 ± 13.0	48.3 ± 14.4	54.5 ± 10.9	58.9 ± 12.2	<0.0001
Familial AGA, n (%) †	405 (38.7%)	145 (37.8%)	46 (33.8%)	85 (38.6%)	63 (40.1%)	66 (44.0%)	0.49
Joint involvement, n (%)	185 (19.8%)	65 (19.0%)	18 (15.1%)	40 (19.9%)	33 (23.4%)	29 (21.8%)	0.51
MetS, n (%)	135 (12%)	38 (7.7%)	15 (11.5%)	22 (9.8%)	23 (14.5%)	37 (24.2%)	<0.0001
Diabete mellitus	117 (10.9%)	33 (8.3%)	14 (10.1%)	17 (7.6%)	18 (11.3%)	35 (22.7%)	<0.0001
Hyperlipidemia	333 (31.0%)	91 (23.2%)	45 (33.1%)	67 (30.0%)	62 (39.5%)	68 (44.4%)	<0.0001
Hypertension	295 (27.5%)	75 (18.9%)	38 (27.7%)	57 (25.6%)	58 (36.5%)	67 (43.8%)	<0.0001
Waist circumference > 94 cm	371 (34.6%)	108 (28.2%)	55 (41.3%)	76 (34.5%)	63 (40.9%)	69 (45.7%)	0.0006

* *Univariate analysis*

Based on a simplified but more stringent definition of MetS (three criteria among hypertension, high waist circumference, diabetes mellitus, and abnormal serum lipid profile) 13.3% (135/1012) of psoriatic patients were considered to have MetS. Of the patients with severe psoriasis (maximal body surface extension >20%) 13.3% had MetS *versus* 10.8% of patients with body surface extension ≤20% of their psoriasis (p = 0.22).

Association of severe AGA with every component of MetS but without statistical significance

In univariate analysis, AGA was highly associated with every component of the MetS (*table 1).* Comparisons between patients with AGA grade 0 *versus* those with AGA grades 3 and 4 were conducted for each component of the MetS by group of ages *(table 2).* In patients older than 59 years, severe AGA was statistically associated with MetS (p = 0.02). Severe AGA was associated with every component of MetS but without statistical significance, as for instance for hyperlipidemia (p = 0.09). Obesity (Body Mass Index ≥30) was significantly associated with severe AGA (p = 0.03). In the other groups of age, severe AGA was not statistically significantly associated with MetS. In the 30-39 year-old patient group, severe AGA was significantly positively associated with hyperlipidemia (p = 0.001). A tendency was found for a positive association between severe AGA and overweight (p = 0.066). In the 40-59 year-old patients group, a significant positive association was demonstrated between severe AGA and high waist circumference (p = 0.069). In multivariate analysis, when adjusted for age, there was no significant association between the severity of AGA and hyperlipidemia (p = 0.30), hypertension (p = 0.50), high waist circumference (p = 0.72), and diabetes mellitus (p = 0.84). But severe AGA was strongly associated with the presence of at least one component of MetS (52.6% *vs* 28.1%, p<0.0001).

Association of AGA with familial history of cardiovascular events

With regard to the association of AGA with a familial history of first degree cardiovascular events, we found a significant positive association between severe AGA and familial history of cardiovascular events (p = 0.02) in patients older than 59 years. In addition, the same positive association was found in the 30-39 year-old group, although it was not significant (p = 0.057). Finally, as expected, a few cardiovascular events were observed in our population and no significant association was demonstrated between AGA and personal cardiovascular events.

Discussion

To the best of our knowledge, this is the first study aiming to assess the prevalence of AGA in psoriatic patients and its association with MetS and its different components. In this large prospective study we confirmed that severity of AGA was associated with each component of the MetS in univariate analysis. After adjustment for age we demonstrated that severe AGA was significantly associated with the presence of at least one component of the MetS in male psoriatic patients. Using our simplified definition for MetS, we only found a positive significant association between severe AGA and MetS in the age group of patients older than 59 years.

Components of the MetS are dyslipidemia, glucose intolerance, insulin resistance, obesity and hypertension. The diagnosis of MetS is established when 3 or more of the five risk determinants are present including in men with a high waist circumference (>102 cm in the United States of America, 94 cm in France), triglycerides ≥150 mg/dL, high-density lipoprotein cholesterol <40 mg/dL, blood pressure ≥130 mmHg/85 mmHg, fasting glucose ≥110 mg/dL [8]. In our study, we used a simplified definition that was more stringent. This definition

Table 2. Cardiovascular diseases and risk factors according to AGA severity and age

All the patients	18-29		30-39		40-49		50-59		> 59		
n = 1,073	AGA 0 n = 78	AGA 3-4 n = 1	AGA 0 n = 83	AGA 3-4 n = 17	AGA 0 n = 88	AGA 3-4 n = 69	AGA 0 n = 84	AGA 3-4 n = 106	AGA 0 n = 56	AGA 3-4 n = 120	p
MetS, n (%)	0 (0)	0 (0)	3 (3.61)	0 (0)	4 (4.6)	1 (1.4)	12 (14.3)	19 (17.9)	11 (19.6)	40 (33.3)	0.02
High waist circumefrence, n (%)	15 (19.2)	0 (0)	39 (47)	7 (41.2)	52 (59.0)	41 (59.4)	51 (59.5)	70 (66.0)	37 (66.1)	88 (73.3)	0.36
Diabetes, n (%)	0 (0)	0 (0)	3 (3.61)	0 (0)	2 (2.3)	3 (4.4)	14 (16.9)	15 (14.3)	14 (25.4)	35 (29.4)	0.58
Hyperlipidemia, n (%)	2 (2.6)	0 (0)	9 (10.8)	7 (43.8)	27 (31.0)	17 (24.6)	27 (32.5)	37 (35.6)	24 (43.6)	69 (57.5)	0.09
Hypertension, n (%)	2 (2.6)	0 (0)	4 (4.8)	2 (11.8)	12 (13.6)	11 (15.9)	27 (32.1)	43 (41.0)	30 (53.6)	69 (57.5)	0.62
Obesity, n (%)	8 (11.1)	0 (0)	14 (16.8)	0(0)	16 (18.2)	12 (35.8)	22 (26.2)	32 (31.4)	12 (21.4)	46 (38.3)	0.03
Smoking, n (%)	35 (45.4)	0 (0)	48 (47.8)	9 (52.9)	58 (65.9)	35 (52.2)	55 (65.5)	63 (59.4)	35 (63.6)	75 (73.3)	0.89
Cardiovascular familial history, n (%)	31 (39.7)	0 (0)	40 (49.4)	9 (52.9)	37 (43)	28 (40.6)	25 (29.8)	46 (44.7)	12 (21.8)	46 (40.2)	0.02
MACE*, n (%)											
Angina pectoris	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.1)	1 (1.4)	2 (2.4)	1 (0.9)	3 (5.4)	13 (10.8)	0.24
Myocardial infarction	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.1)	1 (1.4)	0 (0)	4 (3.8)	3 (5.4)	15 (12.5)	0.11
Stroke	0 (0)	0 (0)	1 (1.2)	0 (0)	1 (1.1)	0 (0)	4 (4.8)	1 (0.9)	1 (1.8)	10 (8.3)	0.17

* *MACE: major adverse cardiovascular events. (): % of patients*

was based on the combination of three criteria among four risk determinants, hypertension, hyperlipidemia, high waist circumference, and diabetes mellitus.

MetS is a strong predictor of cardiovascular diseases, diabetes and stroke, and it significantly increases the risk of cardiovascular mortality. In several population based studies, multiple cardiovascular risk factors, including diabetes mellitus, smoking, obesity, hypertension, and MetS, have been found to be associated with psoriasis [9-11]. In addition, psoriasis has recently been proposed as an independent risk factor for myocardial infarction, especially in young subjects with severe psoriasis [12]. Patients with severe psoriasis have also increased risk of stroke that may not be explained by major stroke risk factors identified in routine medical care [12]. Psoriasis may also be considered as an independent risk for stroke [13].

Our studied population of 1073 patients may be quite representative of French male psoriatic patients treated by dermatologists, as the patients were consecutively recruited from both hospital based dermatology departments and private dermatology practitioners. One of the limitations of our study is that we did not confirm for each patient the prevalence of the different components of the MetS using blood tests, although we confirmed the presence of these components by screening treatments related to MetS. But we confirmed that a high proportion of male psoriatic patients have components of MetS: hypertension, high waist circumference, diabetes mellitus, and abnormal serum lipid profiles were observed in 28%, 59%, 11%, and 31%, respectively. Despite consistent data for the association between psoriasis and cardiovascular risk, a few authors have hypothesized that psoriasis may not be by itself an independent risk factor for cardiovascular disease [14].

Our data suggest that AGA could be considered as a good marker of components of MetS in psoriatic male patients. Others have attempted to search for clinical markers of the MetS in psoriatic patients. Indeed, Gisondi *et al.* proposed to use the Framingham risk score in patients with psoriasis to detect patients at high risk for developing cardiovascular events [15]. This score calculates this absolute risk at 5 and 10 years. It includes age, gender, total cholesterol, high-density lipoprotein cholesterol, systolic blood pressure, smoking status and diabetes mellitus [15]. Apart from other clinical markers of MetS, such as waist circumference and blood pressure, severe AGA could be helpful for the clinician in selecting patients among psoriatic males for blood testing.

The link between AGA and MetS is not well understood. We have previously reported a link between AGA and hypertension and proposed that the mineralocorticoid pathway may be at least partly responsible for the development of AGA [7]. Similarly, in a pilot case-control study, Arias-Santiago *et al.* have confirmed significantly higher systolic blood pressure and plasma aldosterone levels in patients with AGA [16]. Antagonists of mineralocorticoid receptor spironolactone have long been used in the treatment of AGA [17]. Experimental data have demonstrated in transgenic mouse models that overexpression in the skin of mineralocorticoid receptor (aldosterone receptor) may induce alopecia [18]. Interestingly, it has recently been proposed that an increased mineralocorticoid activity could be the common link between obesity, hypertension, hyperlipidemia and insulin resistance. Recent studies have indicated that mineralocorticoid receptor signalling has a pivotal role in MetS-related tissue damages [19-23]. This hypothesis could nicely explain our results, demonstrating a significant association between AGA and the presence of at least one component of MetS, but not of one specific component of MetS. These results are in line with previous reports which found a positive association of AGA and coronary artery disease [24-28]. Indeed, several studies demonstrated a significant association between AGA and coronary artery disease with multivariate analysis but the prevalence of components of MetS or cardiovascular risk factors in patients with AGA was variable: hypertension and a smoking habit [25], smoking habit [26, 27], hypertension and hyperlipidemia [28].

One main result of our study was the association of severe AGA with MetS in the older group of our patients, which argues that AGA may be a good clinical marker of MetS and thus predicts future development of the components of MetS. We did not have information about the onset of development of AGA in our population. Considering our simplified definition based (i) on definite diagnoses of hyperlipidemia and diabetes mellitus, for instance, and (ii) a combination of three components among four, we probably lost a lot of sensitivity in the diagnosis of MetS. We were not able to look for glucose intolerance or dyslipidemia, especially in our younger population, treated by dermatologists "in real life", without strict biologic follow-up.

Interestingly we demonstrated an association between severe AGA and a familial history of cardiovascular events. All together, these results argue for a possible common genetic background predisposing to MetS/cardiovascular risk and AGA.

In conclusion, our study strongly suggests that the presence of severe AGA could be considered as a simple clinical marker for MetS in male psoriatic patients and should thus motivate close monitoring of these patients for the different components of MetS. It would be of interest to confirm this association in larger studies of psoriatic patients in a population-based cohort and to correlate early onset of AGA with the future development of MetS in psoriatic patients. ■

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PELADE SOUS ANTI-TNFα : ETUDE FRANCAISE PROSPECTIVE MULTICENTRIQUE

Tauber M, Buche S, Reygagne P et al.

Alopecia areata occuring during anti-TNF therapy: a national multicenter prospective study

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Afin de recenser la fréquence de survenue d'une pelade sous biothérapie, une étude multicentrique incluant dermatologues, gastro-entérologues et rhumatologues a été réalisée en France du 1er janvier 2011 au 31 décembre 2012.

Le diagnostic de pelade a été confirmé par un dermatologue dans tous les cas.

Au total, 29 patients atteints de pelade ont été recensés : 17 hommes, la moyenne d'âge était de 39,1 ans, 11 étaient atteints de psoriasis, 11 de rhumatismes inflammatoires et 7 de maladies digestives inflammatoires. La présentation prépondérante était une atteinte en plaques atteignant le cuir chevelu ou la barbe. Associées à la pelade, on constatait des lésions de vitiligo, une éruption psoriasique et une thyroïdite d'Hashimoto chez 7 patients (24 %).

La durée moyenne de traitement par anti-TNFa avant l'apparition de la pelade était de 22,5 mois (1 à 89 mois). Les traitements étaient l'infliximab (REMIDADE®) (n : 10), l'adalimumab (HUMIRA®) (n : 11) et l'étanercept (ENBREL®) (n : 8). La majorité des patients à l'exception de 2 étaient de bons répondeurs au traitement. Les anti-TNFa ont été arrêtés chez 14 patients. Une repousse complète ou partielle a été obtenue chez 76 % des patients après une durée moyenne de 5 mois et après un suivi moyen de 24 mois. Il n'y a pas eu de différence pour les repousses entre les patients ayant poursuivi le traitement et ceux l'ayant arrêté.

Après guérison, un patient a eu une rechute sans reprise de l'anti-TNFa et 2 ont récidivé ou se sont aggravés lors du changement de l'anti-TNFa par un autre.

L'imputabilité de l'anti-TNFa dans la survenue de ces pelades est discutable. La pelade peut faire partie des manifestations auto-immunes que l'on est amené à rencontrer chez ces patients au terrain prédisposé ou elle peut correspondre à un effet secondaire auto-immun des anti-TNFa.

Le grand nombre d'hommes dans cette étude, ce qui n'est pas habituel dans la pelade, et le fait qu'1/4 des patients avait d'autres symptômes auto-immuns associés habituellement à la pelade, pourraient laisser à penser que les anti-TNFa soient en cause.

L'évolution identique chez les patients ayant poursuivi le traitement et ceux qui l'ont arrêté n'est pas un argument contre le rôle des anti-TNFa et pour une association fortuite car on peut voir des éruptions psoriasiformes induites par les anti-TNFa évoluer favorablement tout en maintenant le traitement laissant suggérer des voies d'adaptation.

Au total : il ne semble pas nécessaire d'arrêter systématiquement les anti-TNFa lors de la survenue d'une pelade. Une discussion multidisciplinaire apparaît indiquée.

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25	Girard Céline	CHU Montpellier
26	Goujon-Henry Catherine	CHU Lyon Sud
27	Bravard Pierre	Hôpital Jacques Monod, 76083 Le Havre Cedex
28	Reguiai Ziad	CHU Reims, 51092 Reims Cedex
29	Parier Josiane	94210 La Varenne
30	Hamidou Zhor	Hôpital St Louis, Paris
31	Steiner Henri-Georges	38200 Vienne
32	Bastien Marie	94340 Joinville le Pont
33	Halioua Bruno	75 Paris
34	Zeitoun Michèle	92 Antony
35	Maillard Hervé, Beneton Nathalie	CH Le Mans
36	Begon Edouard	Hôpital de Pontoise
37	Bouilly-Auvray Danielle	Service de Dermatologie, CHU Dijon
38	Toussaint Pascal	Hôpital Bagatelle, 33401 Talence Cedex
39	Descamps Vincent	Hôpital Bichat-Claude Bernard, 75018 Paris
40	Géner Gwendeline	91800 Brunoy

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41	Samimi Mahtab	Hôpital Trousseau, CHU Tours
42	Kemula Mathilde	Charenton-Le-Pont, Hôpital Henri Mondor, Créteil
43	Pfister Pierre	75012 Paris
44	Khemis Abdallah	CHU Larchet Nice
45	Devaux Suzanne	Hôpital de Bayonne
46	Barthelme Dominique	Hôpital de Pau
47	Lorier Elisabeth	75015 Paris
48	Barthes Laura	94100 Saint Maur des Fossés, Hôpital Henri Mondor, Créteil
49	Wagner Laurent	75013 Paris
50	Bernier Claire	CHU Nantes
51	De Quatrebarbes Julie	CH Annecy
52	Belon Martine	CMS Pierre Rouquès, 94400 Vitry sur Seine
53	Solyga Bénédicte	94120 Fontenay sous Bois
54	Dominique Lons-Danic	Hôpital Saint-Joseph, Paris
55	Philippe Modiano	Groupe hospitalier Institut Catholique de Lille
56	Pierre-André Becherel	Hôpital Privé d'Antony, 92 Antony