HJOG An Obstetrics and Gynecology International Journal

Review

HJOG 2023, 22 (3), 102-108 | DOI: 10.33574/HJOG.0531

The Role of Lipid Accumulation Product (LAP) as a Metabolic Indicator in Polycystic Ovary Syndrome (PCOS)

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Abstract

Polycystic ovary syndrome (PCOS) presents one of the most widespread endocrine disorders affecting women of reproductive age, predominantly characterized by hyperandrogenism, anovulation, and polycystic ovaries. Women diagnosed with PCOS also present an increased risk for developing metabolic complications like dyslipidemia, metabolic syndrome (MetS) insulin resistance (IR) and type 2 diabetes mellitus. With effective early detection becoming critical to managing these adverse effects, Lipid Accumulation Product (LAP) has emerged as a reliable marker for detecting excessive lipid accumulation beyond adipose tissue, such as in the liver, often associated with cardiometabolic risk; especially among patients with PCOS. This review examines the link between the application of LAP as a predictor of cardiometabolic risks and its association to PCOS, hence seeking possible implementations in clinical settings towards early diagnosis and improved management for affected individuals.

Key words: Lipid accumulation product, polycystic ovary syndrome, PCOS, metabolic syndrome, insulin resistance

Introduction

Polycystic ovary syndrome (PCOS) is an endocrine disorder that affects an estimated 5-20% of women of reproductive age worldwide.[1,2] PCOS is characterized by hyperandrogenism, insulin resistance (IR), and ovarian dysfunction, presenting with a variety of manifestations such as hirsutism, acne, anovulation, and menstrual irregularities.[3,4] Women with PCOS are more likely to develop chronic medical complications, such as type 2 diabetes, cardiovascular disease, and endometrial cancer.[5,6] In addition, PCOS has been linked to metabolic syndrome (MetS) and dyslipidemia, both of which contribute to the elevated cardiovascular risk observed in this population.[7,8]

Assessing lipid overaccumulation is key to pre-

dicting metabolic disorders. An innovative approach among several methods available today is the Lipid Accumulation Product (LAP). Research has shown this index to be a reliable predictor of both IR and cardiometabolic risk. Calculating LAP involves two simple parameters: waist circumference and fasting triglyceride levels, which are easily measurable and inexpensive, without involving risk. LAP formulae are calculated as (waist circumference [cm] – 65) × (triglyceride concentration [mM]) for men, and (waist circumference [cm] – 58) × (triglyceride concentration [mM]) for women.[9] LAP has demonstrated a stronger association with cardiometabolic risk factors and IR than body mass index (BMI), waist-to-hip ratio, and waist circumference alone.[10,11]

The use of LAP has gained attention as a means of assessing metabolic risk among women diagnosed with PCOS. Researchers have found that there is a significant connection between several clinical, hormonal, and metabolic parameters in women suffering from this condition when tested using the LAP method. Therefore, it holds great promise as a diagnostic tool for identifying indications of underlying metabolic dysfunction within this population.[12-14]

Additionally, LAP has been shown to be an independent predictor of IR in women with PCOS, outperforming traditional indices such as BMI and waist circumference.[12,16] A recent meta-analysis also highlights that lifestyle interventions, such as diet and exercise, lead to significant improvements in LAP and cardiometabolic risk factors in women with PCOS.[15] Moreover, LAP has been proposed as a potential marker for monitoring the effectiveness of pharmacological treatments, such as metformin and oral contraceptives, in improving metabolic health in women with PCOS.[17,18]

Furthermore, recent scientific inquiry has focused on comparing the significance of lipid accumulation product (LAP) to other lipid-related indices, such as the visceral adiposity index (VAI), when assessing metabolic or hormonal imbalances amongst women with PCOS.[19-22] The visceral adiposity index (VAI) is a mathematical formula that accounts for waist circumference, body mass index, triglycerides, and HDL cholesterol levels - all factors used for the evaluation of visceral fat distribution and possible metabolic hazards.[21,22] In lean PCOS patients, LAP was reported to be a better predictor of metabolic status than VAI,[19] although both indices were correlated with IR and hyperandrogenemia in obese/overweight women with PCOS.[20] Furthermore, a substantial association was discovered between inflammatory markers and hormonal, metabolic, IR, and obesity indices in first-degree relatives of PCOS patients.[22] These findings show the value of lipid-related indicators in predicting and detecting metabolic and hormonal disorders among women with PCOS across various demographics.

The overarching goal of this review article is to provide an extensive analysis regarding the correlation between LAP and PCOS, by performing a thorough search and critical review of the published research on LAP in women with PCOS, including observational studies, clinical trials, and meta-analyses, aiming to focus on the relevance of LAP as a measure of metabolic risk and IR in this population. Prospective clinical applications of LAP in PCOS care, and gaps and discrepancies in the research that require additional investigation will also be investigated. The findings of this review paper are intended to assist clinicians and researchers in the field gain an improved grasp of the role of LAP in PCOS, with the goal to enhance the care of women with PCOS and limit the long-term health consequences associated with this complex endocrine disorder.

Materials and methods

For this review, the authors searched PUBMED, Google Scholar, MEDLINE (National Library of Medicine, Bethesda, Maryland, MD, USA; January 2000 to May 2023) and the Cochrane Register of Controlled

Trials (The Cochrane Collaboration, Oxford, UK). An electronic search approach included the phrases 'lipid accumulation product (LAP), 'Polycystic Ovary Syndrome (PCOS)'. To find further research of interest, the references of the selected publications and review articles were evaluated. To select possibly relevant papers for this study, the authors evaluated all the citations returned from the computerized search.

Discussion

The growing body of research surrounding the connection between LAP and PCOS, as discussed in this paper, highlights the potential value of LAP as an indicator of metabolic dysfunction and IR within this specific cohort. LAP has demonstrated a stronger association with cardiometabolic risk factors and IR when compared to conventional measures such as BMI, waist to hip ratio and waist circumference alone.[9,11] Given the elevated prevalence of IR and MetS among women with PCOS,[3,4] it becomes imperative to identify straightforward, cost effective and non-intrusive tools like LAP to accurately assess metabolic risk and facilitate effective clinical management.

For this review, we analyzed the significance of LAP as an indicator of metabolic risk and IR in PCOS-affected females. Numerous research studies have established a strong connection between LAP and various clinical, hormonal, and metabolic factors among women diagnosed with PCOS.[12,14] Notably, LAP has been identified as an autonomous predictor of IR within this specific population, surpassing the accuracy of conventional measurements like BMI and waist circumference.[12,16] These compelling findings strongly suggest that LAP possesses the potential to serve as a valuable instrument for identifying women with PCOS who face an elevated risk of developing cardiometabolic complications such as type 2 diabetes and cardiovascular disease.[15]

In a cross-sectional study involving 150 PCOS women and 100 control subjects, Naghshband et al sought to investigate the reliability of LAP in determining the risk of MetS in PCOS. In this study of south Indian PCOS women, the incidence of MetS was 59.3%, which was greater than in other populations. The authors propose LAP as an innovative index for MetS diagnosis in PCOS women, emphasizing the need to establish independent cutoffs for each demographic group.[23]

Lipid accumulation product (LAP) was also tested as a marker of metabolic disturbances (MD) related with IR in young reproductive-aged PCOS patients by Abruzzese et al. In this cross-sectional study, 110 PCOS patients and 88 control participants (aged 18–35) were recruited. Regardless of phenotype, young PCOS patients exhibited higher IR and dyslipidemia. LAP correlated positively with higher BMI, waist circumference, fasting glucose, insulin, triglycerides, and reduced high-density lipoprotein cholesterol levels, making it a more accurate indicator of MD and IR in these women.[24] Additionally, Jabczyk et al. showed a significant association of LAP with metabolic disorders (both glucose/insulin levels and lipid profiles) in PCOS women ($p = 0.000$).[25]

However, despite the body of evidence supporting the utilization of LAP in women diagnosed with PCOS, there remain certain gaps in our comprehension and inconsistencies within the existing literature that require further attention. One area that demands additional investigation is determining the most suitable cutoff values for LAP that accurately predict metabolic risk and IR in women living with PCOS. Different studies have proposed varied thresholds based on specific populations considered, incorporating factors like ethnicity, lifestyle, and other pertinent variables.

Naghshband et al. reported a proposed LAP cut-off value of 53 cm.mmol/L, while Abruzzese et al. a value of 18,24 cm.mmol/L.[23,24] Nascimento et al. examined 78 women in a cross-sectional study, which highlighted that when the lipid accumulation product exceeded 37.9 cm.mmol/L, all cardiovascular risk markers were more likely to change.[26] Hosseinpanah

et al. proposed a cutoff of 34,1 cm.mmol/L.[27]

A study by Xhiang et al aimed to determine whether LAP is capable of recognizing MetS in PCOS women. In this cross-sectional study, 105 PCOS women had their anthropometric, biochemical, and clinical parameters measured. By utilizing receiver operating characteristic (ROC) analysis, the MetS prediction cutoff points for LAP were determined. The prevalence of MetS in the study group was 43.8%. PCOS women with MetS had substantially higher LAP levels than those without it and LAP was strongly correlated with MetS components. LAP was a substantial discriminator for MetS in PCOS women, and the optimal LAP cutoff point for predicting MS was 54.2 (sensitivity: 93.3%, specificity: 96.8%). LAP appears to be associated with MetS and has a high diagnostic sensitivity and specificity for MetS in PCOS women.[28]

Wiltgen et al. intended to determine the reliability of LAP as a predictor of cardiovascular risk in PCOS patients. In a case-control study, 51 PCOS patients aged 14 to 35 years were compared to 44 BMI- and age-matched controls. Included in the measurements were the LAP index, the Homeostatic Model Assessment of Insulin Resistance (HOMA) index, glucose tolerance, plasma hormones, cholesterol, and triglycerides. All subjects exhibited a positive correlation between LAP index and HOMA index (r = 0.70; P 0.001). PCOS patients had greater waist circumference (P = 0.002), HOMA index (P 0.001), and LAP index (P = 0.035) than controls. Based on the analysis of the receiver operating characteristic curve, a LAP index of 34.5 (sensitivity: 84%; specificity: 79%) performed better than non-high-density lipoprotein cholesterol, waist circumference, or body mass index in identifying IR in all subjects. It was confirmed that IR is more prevalent in women with PCOS compared to BMI-matched controls. In addition, the easily accessible LAP index is associated with the HOMA index, and a LAP > or = 34.5 is another indicator of risk for cardiovascular disease in women with PCOS.[29]

Wehr et al. Conducted a study comparing LAP and impaired glucose tolerance (IGT) in 392 PCOS patients and 140 control women of similar age and BMI. After adjusting for age, it was observed that PCOS women had significantly higher LAP levels compared to control women [22.2 (10.9 46.2) and 18.2 (10.7 36.3) respectively, P = 0.001]. In both PCOS and control women, an LAP cutoff value of 44.1 and 41.8 respectively proved to be the most effective in identifying the presence of IGT [sensitivity 79.5%, specificity 80.5%, AUC 0.86 in PCOS women and sensitivity 82.3%, specificity 90.5%, AUC 0.86 in control women]. In conclusion, LAP serves as an easily accessible and cost-effective predictor for predicting IGT in both PCOS and control women.[30]

In a study conducted by Wang et al., the best predictors of IR and hyperandrogenaemia in women with PCOS were investigated. 953 patients with PCOS were separated into two distinct groups based on their body mass index (BMI): normal weight and obesity/overweight. LAP (optimal cut-off value: 45.54, AUC = 0.680) was found to be a sensitive predictor of IR in the obese/overweight population (sensitivity = 72% and sensitivity = 66%). These findings suggested that LAP may aid in the early detection of IR and hyperandrogenaemia in obese/overweight PCOS patients.[31] Another cross-sectional study by Banu et al. examined LAP's relationship with cardiometabolic risk indicators like IR and MetS in 62 newly diagnosed lean PCOS patients and 58 age- and BMI-matched healthy controls. LAP had an excellent discriminating index for MetS in lean PCOS patients.[19]

Additionally, LAP has been recognized as a promising method for evaluating the impact of lifestyle and medication interventions on women with PCOS, aiming to monitor their effectiveness. Lifestyle interventions encompass dietary adjustments and physical activity, which have demonstrated substantial enhancements in LAP and cardiometabolic risk factors

among individuals with PCOS.[17,18] Moreover, LAP holds promise as an indicative measure to track the efficacy of pharmacological treatments like metformin and oral contraceptives in enhancing metabolic well-being among women diagnosed with PCOS. These discoveries emphasize the potential practical implications of LAP in the overall management of PCOS.

Moreover, limited research has been conducted on the role of LAP in predicting long term health complications such as cardiovascular disease and type 2 diabetes among women diagnosed with PCOS. To address this gap, comprehensive longitudinal studies are warranted. Exploring the potential predictive value of LAP in relation to long term health outcomes could aid healthcare professionals in identifying individuals who are at a higher risk of experiencing these complications. This, in turn, would enable them to implement tailored prevention strategies targeted specifically towards those individuals.

Another aspect that remains uncertain is the correlation between LAP and reproductive outcomes among women affected by PCOS. Specifically, exploring whether LAP can function as a predictive marker for pregnancy rates and live births within this population is necessary. Understanding this connection could have significant implications for infertility management in women with PCOS and facilitate appropriate interventions.

It is crucial to acknowledge certain constraints within the existing research literature. First and foremost, it is worth mentioning that a significant portion of the studies analyzed in this review adopted a cross sectional design. This design presents a difficulty in establishing causal relationships between LAP and the various outcomes under investigation. Furthermore, it is important to highlight that most of these studies were conducted in individual centers and featured relatively small sample sizes. As a result, the generalizability of the findings may be restricted due to these factors.

Further research is needed to establish population-specific LAP cutoff values, investigate the association between LAP and reproductive outcomes, and elucidate the predictive value of LAP for long-term health complications in women with PCOS.

To summarize, LAP displays promising potential as a marker for metabolic dysfunction and insulin resistance in women diagnosed with PCOS. It holds promise in identifying individuals who may have a higher likelihood of developing cardiometabolic complications and monitoring the effectiveness of interventions. However, additional research is required to address the gaps and discrepancies in existing studies and establish the practical value of LAP in managing PCOS among women. By enhancing our comprehension of LAP's role in PCOS, we can ultimately contribute to enhancing the overall health outcomes for affected women in the long run.

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Received 09-06-23
Revised 12-06-23
Accepted 16-06-23