Effectiveness of Nonpharmacological Interventions for the Management of Neuropsychiatric Symptoms in Patients With Dementia

A Systematic Review

Liat Ayalon, PhD; Amber M. Gum, PhD; Leilani Feliciano, PhD; Patricia A. Areán, PhD

Background: Recent reports documenting limited evidence supporting the use of pharmacological interventions for neuropsychiatric symptoms (NPS) and increased risk of death, the black box warnings against the use of atypical antipsychotic drugs in older adults, and Omnibus Budget Reconciliation Act regulations suggest the need to evaluate the usefulness of nonpharmacological interventions in the management of NPS of dementia.

Methods: To determine the evidence base of nonpharmacological interventions for the management of NPS in patients with dementia, we reviewed MEDLINE, PsycINFO, the Cochrane library, and relevant bibliographies published from January 1966 to December 2005, using the American Psychological Association Guidelines.

Results: Three randomized controlled trials (RCTs) and 6 single-case designs (SCDs; N of 1 trials) met inclusion criteria. Under unmet needs interventions, 1 SCD found a moderate reduction in problem behaviors. Under behavioral interventions, based on observational data, all 4 SCDs reported a relative reduction of 50% to 100% in neuropsychiatric symptoms. Under caregiving interventions, there were 3 RCTs. At the 6-month follow-up, 1 RCT found a reduction in 4 neuropsychiatric symptom subscales: ideation disturbance score (0.3 vs 0.5; range, 0-8; \( P = .005 \)); irritability score (18.8 vs 23.0; range, 8-38; \( P = .008 \)); verbal agitation, as measured by mean frequency of 20-minute outbursts (0.5 vs 0.8; \( P = .005 \)); and physical aggression score (11.4 vs 12.9; range, 6-42; \( P < .001 \)). Another RCT found a significant improvement in frequency (2.3 vs 3.1; range, 0-4; \( P < .001 \)) and severity (2.2 vs 2.8; range, 0-4; \( P < .001 \)) of target behaviors associated with the intervention arm. The third RCT found no effect. Under bright light therapy, 1 SCD found short-term improvements on the Agitated Behavior Rating Scale (9.7 vs 19.9; \( P < .001 \)).

Conclusions: The cumulative research to date on the impact of nonpharmacologic interventions for NPS among patients with dementia indicates that interventions that address behavioral issues and unmet needs and that include caregivers or bright light therapy may be efficacious. More high-quality research is necessary to confirm these findings.

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assume that NPS are behaviors that have been inadvertently reinforced in the face of an environmental trigger (eg, a patient with dementia learns that he or she can get attention by screaming); and (3) environmental vulnerability and reduced stress-threshold interventions, which assume a mismatch between the person’s environment and their abilities to cope with the situation (and, thus, patients with dementia over-react to their environments; eg, they become agitated by too much noise). Even if the source of NPS is biological, any of these nonpharmacological interventions may still be applied.

Although reviews on nonpharmacological interventions for NPS of dementia exist,10,11 to our knowledge, no previous review has compared the research against the rigorous standards designed by researchers who are expert in the study of nonpharmacological interventions. The conclusions of previous reviews may be inaccurate because of the significant methodological differences between medication trials and nonpharmacological trials. Criteria designed for pharmaceutical studies may ignore the many necessary rigors needed to conduct a fair evaluation of nonpharmacological interventions (such as the use of single-case design methods). In addition, they do not account for the fact that blinded assignment is usually impossible in such interventions because interventionists and patients often are aware of the nature of the intervention (although some participants may be unaware of the intervention owing to dementia). Instead, other methods to overcome these issues, such as blind assessment and intervention manuals, are of major importance.

The American Psychological Association’s Task Force created a set of guidelines to determine whether a nonpharmacological intervention has sufficient evidence.13 The purpose of this review is to compare the existing evidence base for nonpharmacological interventions for NPS with these guidelines so that health care providers, caregivers, and extended care administrators can make informed decisions regarding nonpharmacological management of NPS in patients with dementia. This article complements the study by Sink et al on pharmacological interventions for NPS.

METHODS

SEARCH PROCEDURES

Computer-based searches of MEDLINE, PsycINFO, and the Cochrane library and manual searches of bibliographies identified randomized controlled trials (RCTs) and single-case designs (SCDs; N of 1 trial) testing nonpharmacological interventions for the management of NPS in patients with dementia from January 1966 to December 2005. Key word search criteria combined condition (dementia; Alzheimer, Lewy body, and vascular diseases), nonpharmacological intervention (psychotherapy; behavioral analysis; aroma, behavioral, music, pet, nonpharmacologic, psychotherapy, education, psychosocial, activity, Snoezelen, dance, physical, massage, light, touch, and multisensory therapies; caregiving; contingency management; and restraint-free environment), and outcome (neuropsychiatric disease, hallucination, delusion, combativeness, agitation, aggression, wandering; and behavioral, neurobehavioral, perceptual, psychomotor, and mood disorders).

SELECTION CRITERIA FOR REVIEW

Peer-reviewed English-language studies that tested nonpharmacological interventions for patients with dementia and reported on NPS outcomes were included. We selected only those studies that had as their outcome a reduction in NPS. Similar to the study by Sink et al,1 we did not include studies that evaluated only depression as an outcome but rather focused on disruptive behaviors, such as agitation, aggression, or wandering. (See Teri et al14 for a recent review of psychosocial interventions for the treatment of depression in patients with dementia.)

The APA Task Force identified RCTs and SCDs as the most rigorous designs to assess the efficacy of nonpharmacological interventions. We included RCTs if they (1) randomly assigned participants; (2) compared the intervention with either no treatment or with placebo or attention control, or with some noted standard of care; and (3) used objective measures of outcomes with evidence of validity and reliability. We allowed randomization by site (a minimum of 3 sites per arm) because patient level randomization is not always possible for staff training models. In addition, we included studies that employed a randomized crossover design. This efficient design introduces 2 or more interventions to the same participant in a random order. A washout period is required to diminish potential carryover effects, and only studies with a specified washout period were included. We also included SCDs that compared treatment conditions within an individual across time so that the individual served as his or her own control.

METHODOLOGICAL QUALITY ASSESSMENT

Quality criteria identified by the APA Task Force were used to evaluate the strength of the RCTs and guided the selection of studies we ultimately reviewed. These criteria are that (1) inclusion and exclusion criteria must be clearly stated; (2) there must be a reasonable length of follow-up to determine stability of change; (3) clinical as well as statistical significance should be determined; (4) an agreed-on treatment manual or standard must be used; (5) treatment fidelity must be evaluated; (6) data must be properly analyzed (a between-group comparison and use of intent-to-treat analyses); (7) each cell must have a minimum of 25 subjects; and (8) dropout and treatment refusal information must be clearly documented.

The SCDs needed to meet the following criteria: (1) ABAB (where A denotes no intervention and B, intervention) or multiple baseline designs were allowable because they provide the most compelling evidence of causality (for more detail on these designs, see Kazdin15 and Barlow and Hersen16) (other types of withdrawal designs were not included in this review because we used the strictest interpretation of APA criteria); (2) continuous assessment across phases have been conducted, with a stable baseline assessment of the behavior (at least 3 data points at minimum or predictable variability) established before the intervention was introduced; (3) assessments of NPS were standardized; (4) interobserver agreement (independent agreement between 2 raters) was routinely collected throughout the course of the study (on at least 25% of each phase with a minimum agreement rate of 80%17) to protect against observer drift; and (5) appropriate data analyses were conducted, or in absence of such analyses, graphical presentation of the data was provided. Adopting the strictest interpretation of APA criteria, we included in the analysis only RCTs and SCDs that met all of these criteria.

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DATA ABSTRACTION

Literature searches, as well as data extraction, were conducted independently by at least 2 investigators (L.A., A.M.G., or L.F.). Disagreements between reviewers were discussed, and a consensus agreement was maintained. When necessary, the fourth investigator (P.A.A.) was consulted. To facilitate comparison with Sink et al,1 we used similar abstraction guidelines when possible. These include type of intervention, type of study, number of participants, inclusion and exclusion criteria, dementia type and severity, setting, follow-up period, control group(s), outcome, statistical significance, and clinical significance.

DATA SYNTHESIS

Using the APA guidelines, we classified the interventions into 3 categories. An intervention is determined to be efficacious or evidence-based (1) if there have been 2 independent RCTs that find positive results or (2) multiple replications of SCDs (those with at least 3 subjects each) by 2 or more independent research groups. An intervention is considered possibly efficacious, pending replication, if (1) an SCD has found the intervention to be beneficial in at least 3 participants, (2) if all the RCTs in existence are conducted by 1 team, (3) if there is only 1 RCT in support of the intervention, or (4) if there are equal numbers of positive and negative studies that are of high quality. If none of these conditions is met, then the intervention has no evidence base in a specific population. A treatment is considered to be not efficacious if there have been 3 or more studies and the majority find no treatment effects.

EVIDENCE SYNTHESIS

For a diagram of study flow,17 see the Figure. Three RCTs and 6 SCDs met all APA criteria for contributing to the evidence base and were subsequently reviewed. One SCD was an unmet-needs intervention, 4 SCDs and 3 RCTs were behavioral and learning-based interventions, and 1 SCD was an environmental vulnerability and reduced-stress intervention. See the Table for a summary of study characteristics and findings, organized by study type.

EVIDENCE FOR UNMET-NEEDS INTERVENTIONS

These interventions assess the motivation behind the NPS and design an intervention to either prevent the NPS from occurring or reduce their intensity. Thus, the intervention is tailored specifically to the patient. One SCD met our quality criteria. This study found that of the 2 to 4 most frequent and upsetting behaviors identified by caregivers based on the Behavior Pathology in Alzheimer Disease Scale, there was an improvement in at least 1 problem behavior for all 8 participants and an improvement in 2 to 4 problem behaviors for 6 of the participants.18 Because only 1 SCD was reviewed and resulted in positive outcomes, this intervention is possibly efficacious, pending replication of findings.

EVIDENCE FOR LEARNING AND BEHAVIORAL MODELS

We further divided this category into 2 subcategories based on the focus of the intervention. Behavioral interventions focus primarily on changing the frequency and/or duration of NPS through changes in the environment. Caregiving interventions focus on teaching caregivers of patients with dementia techniques for managing NPS and how to deal with the stress associated with caregiving.

BEHAVIORAL INTERVENTIONS

Four SCDs qualified for the review.19-22 These interventions manage NPS through contingency management such as removing rewards (eg, giving attention for NPS), delivering rewards for prosocial behaviors, or behavioral redirection. Based on observational data, all SCDs found a significant reduction in disruptive behaviors following intervention (a reduction of 80% or more in out-of-seat behavior intervals [mean percentage of out-of-seat behavior intervals at baseline, 18.3%; mean percentage of intervals following intervention, 3.85%] and agitated speech [mean percentage of agitated speech intervals at baseline, 33.7%; mean percentage of intervals following intervention, 9.6%])19, 95% reduction in entry into a restricted area (mean entries per hour at baseline, 7.6; mean entries following intervention, 0.4)20; a 50% to 80% reduction in wandering frequency across participants;21 a 100% reduction in physical and/or verbal aggression during treatment phase across participants (number of agitated assaults ranged from 1 to 3 at baseline).22 Because of the limited scale of these SCDs and given their positive outcomes, individualized behavioral interventions are possibly efficacious, pending further research.

CAREGIVING INTERVENTIONS

Caregiving interventions provide education and support to caregivers of patients with dementia and assistance in managing NPS by using unmet needs and behavioral in-
interventions. Three RCTs23-25 met all APA quality criteria. At the 6-month follow-up, 1 RCT24 found a significant group difference of small to medium magnitude in scores of 4 subscales: (1) the Ideation Disturbance scale of the Cornell Scale for Depression in Dementia scores (range, 0-8) (mean [SD] under intervention arm, 0.3 [0.9]; mean [SD] under control treatment arm, 0.5 [1.6]; P = .005); (2) the Irritability Scale of the Multidimensional Observation Scale for Elderly Subjects (range, 8-38) (mean [SD] under intervention arm, 18.8 [9.6]; mean [SD] under control treatment arm, 23.0 [17.1]; P = .008), (3) the Cohen Mansfield Agitation Inventory Verbally Agitated Scale (frequency of verbal agitation during a 20-minute period) (mean [SD] under intervention arm, 0.5 [1.2]; mean [SD] under control treatment arm, 0.8 [2.8]; P = .005), and (4) the Physically Nonaggressive Scale (range of scores, 6-42) (mean [SD] under intervention arm, 11.4 [7.4]; mean [SD] under control treatment arm, 12.9 [6.2]; P < .001) relative to usual care. However, the RCT conducted multiple comparisons, and the effect size was small to medium. There also was a possibility of regression to the mean because baseline values of usual care seemed to be lower than the intervention’s baseline values. Another RCT found that of 3 problem behaviors identified by caregivers, there was an improvement in at least 1 for all participants in the treatment group immediately after intervention as well as a significant improvement in frequency (range, 0-4; mean [SD] frequency of problem behaviors at baseline, 3.1 [0.7]; mean [SD] postintervention, 2.3 [0.8]; P < .001) and severity (range, 0-4; mean [SD] severity of problem behaviors at baseline, 2.8 [0.6]; mean [SD] postintervention, 2.2 [0.8]; P < .001) of target behaviors but no group differences at follow-up.24 A third RCT found no effect on NPS.25

Given the mixed results, caregiving interventions are possibly efficacious, pending replication.

<table>
<thead>
<tr>
<th>Study and Type of Study</th>
<th>Intervention</th>
<th>Participants, No.</th>
<th>Exclusion/Inclusion</th>
<th>Dementia Type and Severity Setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palmer et al26</td>
<td>Hearing aids</td>
<td>10 CG/pt dyads 8 postintervention</td>
<td>CG: MMSE ≥26; pt MMSE 13-23; hearing loss; live with CG, no neurological hx, speak English</td>
<td>AD, mild to moderate CD</td>
</tr>
<tr>
<td>Bakke et al27</td>
<td>Multicomponent: functional analysis, contingent reinforcement, breaks, time and task feedback; 23 sessions</td>
<td>1 Agitation, wandering</td>
<td>Moderate AD; MMSE = 9</td>
<td>Home</td>
</tr>
<tr>
<td>Feliciano et al28</td>
<td>CB, redirection, minimal attention 4 mo</td>
<td>1</td>
<td>Dementia, referred by staff for wandering</td>
<td>Adult day care</td>
</tr>
<tr>
<td>Heard and Watson29</td>
<td>DRO, individualized reinforcers</td>
<td>4</td>
<td>Dementia</td>
<td>NH</td>
</tr>
<tr>
<td>Moniz-Cook et al30</td>
<td>Functional analysis, removal of individual triggers; 16 d to 7 wk</td>
<td>5 (2 had ABAB design)</td>
<td>Dementia</td>
<td>RH or NH</td>
</tr>
<tr>
<td>McCallion et al31</td>
<td>FVEP: 4 1.5-h group sessions, 3 1-hr family conferences over 8 wk to improve family communication</td>
<td>66 dyads (57 postintervention)</td>
<td>Dementia, GDS ≥3, displayed problem behavior per staff, regular family/friend visitor (known resident ≥2 y)</td>
<td>MMSE mean = 5.81 (tx), 7.97 (control)</td>
</tr>
<tr>
<td>Teri et al32</td>
<td>CG training in behavior mgmt by community consultants; 8 weekly sessions and 4 monthly telephone calls</td>
<td>95 dyads (83 postintervention)</td>
<td>CG: spouse or adult relative Pt: ADRD, ≥3 agitated and depressed behavioral problems ≥3/wk per CG</td>
<td>ADROMMSE mean = 14.7 CD</td>
</tr>
<tr>
<td>Teri et al33</td>
<td>CG trained in behavior mgmt and exercise program for pt, 12 1-hr sessions in 3 mo and 3 monthly follow-ups</td>
<td>153 dyads (140 postintervention, 89 at 24-mo postintervention)</td>
<td>AD community dwelling, ambulatory, CG consent</td>
<td>AD MMSE mean = 16.8</td>
</tr>
<tr>
<td>Lovell et al34</td>
<td>BLT (2500 lux, 2 h each morning) 3-d baseline, 10-d tx, 36 d total</td>
<td>6</td>
<td>Resident ≥3 mo, some agitation, judged adjusted to facility, not blind</td>
<td>Moderate to severe Skilled nursing facility</td>
</tr>
</tbody>
</table>

(continues)
Table. Study Characteristics and Outcomes (cont)

<table>
<thead>
<tr>
<th>Study and Type of Study</th>
<th>Assessment Periods</th>
<th>Control Group</th>
<th>Outcome</th>
<th>Unmet Needs Intervention</th>
<th>Learning and Behavioral Interventions</th>
<th>Caregiving Interventions</th>
<th>EN/RST: BLT Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palmer et al,24 SCD-MBD</td>
<td>6-10 wk baseline, ongoing for 5 mo</td>
<td>UC</td>
<td>Hearing aid use, Behave-AD score</td>
<td>≥1 Problems improved for all, 2-3 problems improved for 6 pt</td>
<td>No SA</td>
<td>No SA</td>
<td>Yes</td>
</tr>
<tr>
<td>Bakke et al,19 SCD-ABAB</td>
<td>Baseline; in-session</td>
<td>Baseline (UC)</td>
<td>Out of seat and agitated speech</td>
<td>No SA</td>
<td>Yes, reduced &gt;80% for both behaviors</td>
<td>Yes, reduced 50%-80% across participants</td>
<td>Yes, no behavior incidents during tx phases</td>
</tr>
<tr>
<td>Feliciano et al,20 SCD-ABAB, component analysis, stimulus fading</td>
<td>Ongoing for 4 mo</td>
<td>Baseline (UC)</td>
<td>Decrease in number of entries into office</td>
<td>No SA</td>
<td>Yes, 95% reduction for CB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heard and Watson,21 SCD-ABA</td>
<td>6-9 Baseline sessions, each tx session 12-24 mo</td>
<td>Baseline (UC)</td>
<td>Wandering frequency</td>
<td>No SA</td>
<td>Yes, reduced 50%-80% across participants</td>
<td>Yes, no behavior incidents during tx phases</td>
<td></td>
</tr>
<tr>
<td>Moniz-Cook et al,22 SCD-ABA or ABAB</td>
<td>Baseline (UC)</td>
<td>Behavioral observation; naturalistic observation by staff; review of records; interviews</td>
<td>No SA</td>
<td>No SA</td>
<td>No SA</td>
<td>No SA</td>
<td></td>
</tr>
<tr>
<td>McCaillen et al,23 RCT, blind (randomized within NH)</td>
<td>3 mo, 6 mo</td>
<td>UC</td>
<td>MOSES (staff), CSDD (staff and resident), CMAI-O, CMAI-nurse, minutes spent managing problem behavior (staff), psychotropic drug and restraint use</td>
<td>No group differences at 6-mo in problem behavior; postintervention: 100% in tx reported some improvement in ≥1 target behavior</td>
<td>Possible, but small differences and multiple comparisons, possibly regression to the mean</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Teri et al,24 RCT, blind</td>
<td>Baseline, 2 mo (post-tx), 6-mo follow-up</td>
<td>UC</td>
<td>3 Target behaviors, NPI, RMBPC reaction</td>
<td>No group differences at 6-mo in problem behavior; postintervention: 100% in tx reported some improvement in ≥1 target behavior</td>
<td>Yes for frequency (before and after comparison; postintervention) but no group difference at 6 mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Teri et al,25 RCT, blind</td>
<td>Baseline, 3 mo (postintervention), 6 mo, 12 mo, 18 mo, 24 mo</td>
<td>UC</td>
<td>CSDD, RMBPC</td>
<td>Tx group improved CSDD, NS for RMBPC, inst, but fewer inst for behavior in tx group (19%) vs UC (50%)</td>
<td>No, trend for institutionalization but not for RMBPC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lovell et al,26 SCD-ABABA</td>
<td>Every 15 min, 4-8 PM</td>
<td>UC</td>
<td>ABRS</td>
<td>Agitation scores significantly lower during tx; F1,25 = 14.40; P &lt; .001</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: ABAB, A = no intervention, B = intervention; ABRS, Agitated Behavior Rating Scale; AD, Alzheimer disease; ADL, activities of daily living; ADRD, Alzheimer disease and related disorders; Behave-AD, Behavior in Alzheimer Disease scale; BLT, bright light therapy; CB, cloth barrier; CD, community dwelling; CG, caregiver; CMAI, Cohen-Mansfield Agitation Inventory; CMAI-O, Cohen-Mansfield Agitation Inventory Observer-derived; CSDD, Cornell Scale for Depression in Dementia; DRO, differential reinforcement of other behaviors; dx, diagnosis; EN, environmental vulnerability; FVEP, Family Visit Education Program; GDS, Global Deterioration Scale; hx, history; IADL, Instrumental Activities of Daily Living; inst, institutionalization; ITT, intention to treat; MBD, multiple baseline design; mgmt, management; MMSE, Mini Mental State Examination; MOSES, Multidimensional Observation Scale for Elderly Subjects; NHs, nursing homes; NPI, Neuropsychiatric Inventory; pt, patient; RCT, randomized controlled trial; RH, residential home; RMBPC, Revised Memory and Behavior Problem Checklist; RST, reduced threshold; SA, statistical analysis; SCD, single-case design; tx, treatment; UC, usual care.

EVIDENCE FOR ENVIRONMENTAL VULNERABILITY AND REDUCED STRESS-THRESHOLD MODELS

One type of reduced stress-threshold model met criteria for review: bright light therapy, which is based on the premise that exposure to direct bright light produces a calming effect on the agitated patient. Only 1 SCD26 met inclusion criteria. Based on the Agitated Behavior Rating Scale (ABRS), agitation was significantly lower with the bright light condition (mean score on the ABRS under the no-intervention arm, 19.93; mean score on the ABRS under the intervention arm, 9.71; P < .001); however, the effects did not last beyond 1 day after intervention (mean score on the ABRS, 19.19). Thus, bright light therapy is possibly efficacious, pending replication of findings.

COMMENT

This review revealed a number of interesting findings regarding the state of research on nonpharmacological interventions for NPS. The most striking finding was an unintended one: although several hundred studies have investigated the efficacy of these interventions, only a handful met all APA criteria for quality of method, and of those, most were SCD
Though the possibility of publica-
verse effects. Furthermore, al-
studies reviewed did not evaluate ad-
search is the fact that most of the
stakes among staff and family care-
important issues about the need for
changes to be published than negative find-
ings from RCTs.
As we await more sophisticated re-
search, clinicians are left with guide-
lines that clearly state that medica-
tions should be used as a last resort
and that nonpharmacological ap-
proaches should be used first. The
best clinical research to date sup-
ports an individualized approach, in
which potential causes of the symp-toms are identified and addressed ac-
cording to behavioral techniques. Such causes may include pain, fat-
tigue, and other physical symp-toms; understimulation or overstimu-
lation; or environmental triggers. A
careful functional analysis of the be-
behavior and its antecedents and con-
sequences is a crucial aspect of such
behavioral interventions. This
type of individualized approach re-
quires an interdisciplinary team ap-
proach and careful assessment and
reassessment to ensure optimal out-
comes. Educating caregivers about
how to manage NPS as well as their
own distress also is an important as-
pect of such multimodal care and has
shown modest improvements.

To our knowledge, the present re-
view is the only one to have used the
most rigorous evaluation criteria de-
veloped specifically for behavioral in-
terventions and as such constitutes
the most in-depth analysis of the re-
search to date on nonpharmacologi-
cal management of NPS. Given the
fact that other reviews that included
studies of varying quality of method
concluded that many of these inter-
ventions are promising, future re-
search will be extremely worthwhile
to determine the efficacy of nonpharmacological methods of NPS
management. In addition, more work
is needed to determine the most fea-
sible outcome for patients with de-
mentia. Of the interventions in exist-
ence, the most promising (although
still requiring further evidence) seem
 to be individually tailored behav-
ioral interventions.

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Correspondence: Liat Ayalon, PhD,
School of Social Work, Bar Ilan Uni-
versity, Faculty of Social Sciences,
Ramat Gan 52900, Israel (layalon
@iit.edu).
Author Contributions: Study con-
cept and design: Ayalon, Gum, and
Areán. Acquisition of data: Ayalon,
Gum, and Feliciano. Analysis and in-
terpretation of data: Ayalon, Gum,
Feliciano, and Areán. Drafting of the
manuscript: Ayalon, Gum, and Ar-
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ten: Ayalon, Gum, Feliciano, and
Areán.
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