11C- or 18F-Choline PET/CT for Imaging Evaluation of Biochemical Recurrence of Prostate Cancer

Paola Mapelli1, Elena Incerti1, Francesco Ceci2, Paolo Castellucci2, Stefano Fanti2, and Maria Picchio1

1Unit of Nuclear Medicine, IRCCS San Raffaele Scientific Institute, Milan, Italy; and 2Unit of Nuclear Medicine, S. Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy

Recurrence of prostate cancer is suspected when an increase in the prostate-specific antigen level is detected after radical treatment; the recurrence could be local relapse, distant relapse, or both. Differentiation between the two patterns of relapse is critical for choosing the proper treatment strategy. Choline PET/CT could be of help in discriminating patients with local, lymph node, and bone recurrences, thus having an impact on patient management.

Key Words: prostate cancer; biochemical recurrence; 11C-choline; 18F-choline; PET/CT

DOI: 10.2967/jnumed.115.169755

After radical treatment for prostate cancer (PCAs), prostate-specific antigen (PSA) is a sensitive biomarker indicating the presence of recurrent disease. However, it does not provide information regarding the sites of recurrent disease, which is mandatory for correct treatment planning (1). PET/CT with a choline tracer radiolabeled with either 11C (11C-choline) or 18F (18F-choline) has been successfully used to identify and localize recurrences of PCAs. The rate of detection by choline PET/CT may vary according to the PSA level, with a higher accuracy for PSA levels of greater than 1 ng/mL. However, recent data also showed the potential of this imaging modality in patients experiencing low PSA levels (<1 ng/mL) (2,3). Recently, European Association of Urology guidelines (4) suggested the use of choline PET/CT in patients with biochemical relapse (BR) and PSA levels of 1–2 ng/mL. The main advantage of choline PET/CT in recurrent PCAs is represented by the possibility of detecting distant metastases (Fig. 1), thus influencing patient management, especially for patients with a single site of disease or oligometastatic disease.

This review provides an overview of the diagnostic performance of 11C-choline and 18F-choline PET/CT in detecting local, lymph node, and bone recurrences, with a specific focus on the influences of PSA levels and PSA kinetics.

METHODS

A comprehensive PubMed literature search up to February 2016 was performed, and articles related to 11C-choline and 18F-choline PET/CT in BR of PCAs were identified. Search terms used to identify such articles were “PET” or “PET/CT,” “11C-choline,” “18F-choline,” “prostate cancer,” “biochemical recurrence,” and “recurrent.” Original publications, meta-analyses, and reviews were selected for inclusion in this review. Table 1 and Table 2 show studies reporting the sensitivity and specificity of 11C-choline and 18F-choline, respectively, in recurrent PCAs, for a total of 36 studies and 3,493 patients.

11C-CHOLINE PET/CT IN RECURRENT PCA

Local Recurrence

The available data regarding the diagnostic performance of 11C-choline PET/CT in detecting local recurrence in patients with BR are limited and controversial. Reske et al. evaluated the role of 11C-choline PET/CT in 36 patients with biopsy-proven low-volume local recurrence after radical prostatectomy (RP), reporting a sensitivity and a specificity of 73% and 88%, respectively (5). Souvatzoglou et al. found 11C-choline uptake in the prostatic bed in 7 of 37 patients (19%) who had PSA failure after RP and were candidates for salvage radiotherapy (RT) of the prostastic fossa (6). These data were substantially confirmed by Kitajima et al., who found a sensitivity of 54% and a specificity of 92% for 11C-choline PET/CT in the detection of local relapse in 87 patients after RP (7).

Lymph Node Recurrence

Few prospective studies investigating the accuracy of 11C-choline PET/CT in detecting lymph node metastases in patients with BR and having histopathology as a reference standard are currently available. One of the first studies was performed by Scattoni et al. (8). Using a per-lesion analysis, they found sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of 64%, 90%, 86%, 72%, and 77%, respectively, for 11C-choline PET/CT (8). Similar results were reported by Schilling et al. (9) and Rinnab et al. (10), supporting the use of 11C-choline PET/CT in patients with BR and suspected lymph node metastases. Kitajima et al. compared 11C-choline PET/CT results with multiparametric MRI results in 115 patients with BR after RP (7). They reported patient-based sensitivity, specificity, and accuracy of 90%, 100%, and 93%, respectively, for 11C-choline PET/CT in the detection of lymph node recurrence; with MRI, sensitivity, specificity, and accuracy for pelvic nodal involvement were 64%, 85%, and 70%, respectively (7).

Bone Metastases

11C-choline PET/CT is an imaging modality that can be useful in detecting bone metastases. Fuccio et al. compared 11C-choline...
PET/CT and bone scanning in 25 patients who had BR and only 1 bone lesion on bone scanning (11). 11C-choline PET/CT detected multiple sites of bone relapse in 44% of the patients, with a sensitivity and a specificity of 86% and 100%, respectively (11). A direct comparison of 11C-choline PET/CT and bone scanning was performed by Picchio et al. in 78 patients with PSA progression after primary treatment (12). They found a lower sensitivity for 11C-choline PET/CT than for bone scanning (98% vs. 100%) but a higher specificity (98% vs. 75%) (12). Ceci et al. used 11C-choline PET/CT to study 304 bone lesions (184 osteoblastic, 99 osteolytic, and 21 bone marrow lesions) in 140 patients during BR (13). They found a significant difference in the SUVmax between osteoblastic lesions (lower values) and osteolytic lesions (higher values) (13).

**INFLUENCE OF PSA ON RATE OF DETECTION BY 11C-CHOLINE PET/CT**

Various studies have investigated the diagnostic accuracy of 11C-choline PET/CT for detecting PCa recurrence and have reported different values for sensitivity and specificity (5,7–9,11,12,14). These variations could be attributed to the heterogeneity of patient populations in terms of inclusion criteria (i.e., PSA level, staging, and presence or absence of androgen deprivation therapy [ADT]). In addition to the largely documented influence of serum PSA measurement on the rate of detection of PCa recurrence by 11C-choline PET/CT (10,14,15), several studies have reported that PSA kinetics, including PSA doubling time (PSAdt) and PSA velocity (PSAvel), are strong predictors for positive PET scan results.

Castellucci et al. investigated 190 patients with BR, subdividing the population into different groups according to trigger PSA levels, and identified an optimal PSA level of 2.43 ng/mL for detecting recurrent disease with a sensitivity and a specificity of 73% and 96%, respectively (16). The same group found that 11C-choline PET/CT results were positive in 28% of 102 patients who experienced only slight increases in PSA levels (<1.5 ng/mL), with 7 patients having local recurrence, 13 having bone metastases, and 9 having lymph node relapse (17).

Using a larger cohort of patients, Giovacchini et al. found a patient-based sensitivity of 85%, specificity of 93%, and accuracy of 89% for 11C-choline PET/CT in the detection of recurrent disease in 358 patients previously treated for PCa (18). As expected, the rate of positive scan results increased with increasing PSA levels (19% for PSA levels of 0.23–1 ng/mL, 46% for PSA levels of 1–3 ng/mL, and 82% for PSA levels of >3 ng/mL); the optimal PSA level was identified as 1.4 ng/mL (sensitivity, 73%; specificity, 72%) (18). Using a cohort of 170 patients with BR of PCa, the same group demonstrated that—like PSA—PSAdt is an independent predictor for 11C-choline PET/CT (19).

Rybalov et al. evaluated 185 patients with BR to assess the impact of PSA levels and PSA kinetics on rates of detection by 11C-choline PET/CT (20). A significant difference in the area under the curve was observed between total PSA (0.721; \( P < 0.001 \)) and PSAvel (0.730; \( P < 0.001 \)) (20). Moreover, detection rates were less than 50% for PSA levels of less than 2 ng/mL or PSAvel of less than 1 ng/mL (20). Bertagna et al. suggested that the highest accuracy for patients with BR and treated only with RT is reached when 11C-choline PET/CT is performed above a cutoff value for PSA of 2.0 ng/mL (21). Mamede et al. evaluated the role of 11C-choline in 71 patients who had BR after RP and a PSA level of less than 0.5 ng/mL and found true-positive findings in 21.1% of the patients (22). The mean ± SD PSA level, PSAdt, and PSAvel for patients with 11C-choline PET/CT–positive results were 0.37 ± 0.1 ng/mL, 3.4 ± 2.1 mo, and 0.05 ± 0.1 ng/mL/y, respectively (22). Interestingly, only PSAdt and the ongoing hormonal treatment were statistically significant in the prediction of positive PET/CT scan results in a multivariate analysis (22). Mitchell et al. evaluated the performance of 11C-choline PET/CT in 176 patients with BR after treatment and found sensitivity, specificity, PPV, and NPV of 93%, 76%, 91%, and 81%, respectively (23). Moreover, the optimal PSA level for lesion detection was shown to be 2.0 ng/mL, and a multivariate analysis demonstrated that PSA (hazard ratio, 1.37; \( P = 0.04 \)) and clinical stage at initial diagnosis (hazard ratio, 5.19; \( P = 0.0035 \)) were significant predictors of positive 11C-choline PET/CT scan results (23). In a recent metaanalysis, Fanti et al. reported a 11C-choline PET/CT rate of detection of PCa at any site of relapse of 62% (95% confidence interval, 53%–71%), a pooled sensitivity of 88% (95% confidence interval, 83%–93%), and a pooled specificity of 87% (95% confidence interval, 71%–95%); these results were similar to previously reported results (24).

**11F-CHOLINE PET/CT IN RECURRENT PCA**

**Local Recurrence**

As for 11C-choline PET/CT, limited diagnostic accuracy of 11F-choline PET/CT in detecting local recurrence has been reported. Using 11F-choline and 11C-acetate PET/CT in a small cohort of 22 patients referred for salvage or adjuvant RT, Veer et al. observed a rate of detection of 55% for PSA levels of less than 1 ng/mL (25). In that study, MRI results were positive in 83% of the patients; this finding suggested that MRI may be more useful than PET/CT in patients with a low likelihood of distant metastases because the sensitivity and specificity of PET/CT were too low to justify its use as a standard diagnostic imaging modality for identifying early relapse (25). Panebianco et al. compared MRI performance and 11F-choline
PET/CT performance in patients with PCa recurrence (26). The population was subdivided into 2 groups: group A, including 28 patients with lesion sizes of 5–7.2 mm and a reduction in PSA levels after RT, and group B, including 56 patients with lesion sizes of 7.6–19.4 mm. In group A, the sensitivity, specificity, PPV, and accuracy of PET/CT in identifying local recurrence were 62%, 50%, 88%, and 60%, respectively (26). The diagnostic performance of MRI was better, given that the sensitivity, specificity, PPV, and accuracy were 92%, 75%, 96%, and 89%, respectively (26). Also, in group B, the performance of PET/CT was poorer than that of MRI, given that the sensitivity, specificity, PPV, and accuracy of PET/CT were 92%, 33%, 98%, and 91%, respectively, whereas those of MRI were 94%, 100%, 100%, and 94%, respectively (26).

Lymph Node Recurrence

Few of the studies currently available have assessed the role of 18F-choline PET/CT in detecting recurrence in the lymph nodes. Husarik et al. studied 111 patients who had PCa and underwent 18F-choline PET/CT; 68 of these patients underwent this scan for the purpose of restaging (27). Local recurrence was correctly identified in 36 of 68 patients (27). Twenty-three patients had 18F-choline lymph node uptake, and in 20 of these 23 patients, lymph nodes were surgically removed (27). Histopathology confirmed metastases in all lymph nodes.

### TABLE 1

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>No. of patients</th>
<th>Type of data collection</th>
<th>No. of patients</th>
<th>Type of data collection</th>
<th>PSA (ng/mL)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Assessed parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>de Jong et al. (43)</td>
<td>2003</td>
<td>36</td>
<td>Prospective</td>
<td>NA</td>
<td>Quantitative analysis</td>
<td>64</td>
<td>100</td>
<td>89</td>
<td>LR, N, B</td>
</tr>
<tr>
<td>Scattoni et al. (48)</td>
<td>2007</td>
<td>25</td>
<td>Prospective</td>
<td>1.98</td>
<td>Quantitative analysis</td>
<td>0.23–23.12</td>
<td>100</td>
<td>66</td>
<td>N</td>
</tr>
<tr>
<td>Rinnab et al. (40)</td>
<td>2007</td>
<td>50</td>
<td>Retrospective</td>
<td>2.42*</td>
<td>Quantitative analysis</td>
<td>0.5–13.1</td>
<td>95</td>
<td>40</td>
<td>LR, N, B</td>
</tr>
<tr>
<td>Schilling et al. (9)</td>
<td>2008</td>
<td>10</td>
<td>Retrospective</td>
<td>1.0±1.5</td>
<td>Quantitative analysis</td>
<td>0.7–1.4</td>
<td>75</td>
<td>93</td>
<td>N</td>
</tr>
<tr>
<td>Krause et al. (44)</td>
<td>2008</td>
<td>63</td>
<td>Retrospective</td>
<td>2.15</td>
<td>Quantitative analysis</td>
<td>0.2–39</td>
<td>36/43/62/73</td>
<td>NA</td>
<td>LR, N, B</td>
</tr>
<tr>
<td>Reske et al. (5)</td>
<td>2008</td>
<td>36</td>
<td>Retrospective</td>
<td>2.0±2.0</td>
<td>Quantitative analysis</td>
<td>0.3–12.1</td>
<td>73</td>
<td>88</td>
<td>LR</td>
</tr>
<tr>
<td>Rinnab et al. (40)</td>
<td>2009</td>
<td>41</td>
<td>Retrospective</td>
<td>2.1</td>
<td>Quantitative analysis</td>
<td>0.41–11.6</td>
<td>93</td>
<td>36</td>
<td>LR, N, B</td>
</tr>
<tr>
<td>Castellucci et al. (6)</td>
<td>2009</td>
<td>190</td>
<td>Retrospective</td>
<td>2.1</td>
<td>Quantitative analysis</td>
<td>0.2–25.4</td>
<td>73**</td>
<td>69**</td>
<td>LR, N, B, M</td>
</tr>
<tr>
<td>Giovacchini et al. (18)</td>
<td>2010</td>
<td>358</td>
<td>Retrospective</td>
<td>1.27</td>
<td>Quantitative analysis</td>
<td>0.23–45</td>
<td>85</td>
<td>93</td>
<td>LR, N, B</td>
</tr>
<tr>
<td>Giovacchini et al. (19)</td>
<td>2010</td>
<td>170</td>
<td>Retrospective</td>
<td>1.25</td>
<td>Quantitative analysis</td>
<td>0.23–48.6</td>
<td>87</td>
<td>89</td>
<td>LR, N, B</td>
</tr>
<tr>
<td>Fuccio et al. (11)</td>
<td>2010</td>
<td>25</td>
<td>Retrospective</td>
<td>6.3</td>
<td>Quantitative analysis</td>
<td>0.2–37.7</td>
<td>86</td>
<td>100</td>
<td>B</td>
</tr>
<tr>
<td>Breeuwsma et al. (15)</td>
<td>2010</td>
<td>70</td>
<td>Prospective</td>
<td>10.7</td>
<td>Quantitative analysis</td>
<td>0.6–54.7</td>
<td>81</td>
<td>100</td>
<td>LR, N, B</td>
</tr>
<tr>
<td>Bertagna et al. (21)</td>
<td>2011</td>
<td>210</td>
<td>Retrospective</td>
<td>5.9±1.9</td>
<td>Quantitative analysis</td>
<td>19.6±19.6</td>
<td>77</td>
<td>93</td>
<td>LR</td>
</tr>
<tr>
<td>Castellucci et al. (17)</td>
<td>2011</td>
<td>102</td>
<td>Retrospective</td>
<td>0.93</td>
<td>Quantitative analysis</td>
<td>0.67–1.1</td>
<td>93±1.1</td>
<td>74±1.1</td>
<td>LR</td>
</tr>
<tr>
<td>Picchio et al. (12)</td>
<td>2012</td>
<td>78</td>
<td>Retrospective</td>
<td>2.4</td>
<td>Quantitative analysis</td>
<td>0.2–500</td>
<td>89</td>
<td>98</td>
<td>B</td>
</tr>
<tr>
<td>Mitchell et al. (23)</td>
<td>2013</td>
<td>176</td>
<td>Retrospective</td>
<td>7.2</td>
<td>Quantitative analysis</td>
<td>2.2–1028</td>
<td>93</td>
<td>76</td>
<td>LR, N, B, M</td>
</tr>
<tr>
<td>Rybalov et al. (20)</td>
<td>2013</td>
<td>185</td>
<td>Retrospective</td>
<td>18.45±2.0</td>
<td>Quantitative analysis</td>
<td>80±54</td>
<td>65±54</td>
<td>89</td>
<td>LR, N, B, M</td>
</tr>
<tr>
<td>Mamede et al. (22)</td>
<td>2013</td>
<td>71</td>
<td>Retrospective</td>
<td>0.34±0.1</td>
<td>Quantitative analysis</td>
<td>0.1–0.5</td>
<td>88</td>
<td>98</td>
<td>LR, N, B, M</td>
</tr>
<tr>
<td>Kitajima et al. (7)</td>
<td>2014</td>
<td>115</td>
<td>Retrospective</td>
<td>2.5</td>
<td>Quantitative analysis</td>
<td>0.58–86.3</td>
<td>54</td>
<td>92</td>
<td>LR</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>90</td>
<td>100</td>
<td>N</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>81</td>
<td>99</td>
<td>B</td>
</tr>
</tbody>
</table>

*Positive scan results.
†Negative scan results.
‡Mean.
§Negative histologic results.
||Positive histologic results.
|Expressed as rate of detection. The different sensitivity values are for different PSA levels: 36 for PSA less than 1, 43 for PSA between 1 and 2, 62 for PSA between 2 and 3, and 73 for PSA 3 or higher.
#PSA level in control patients was 0.1 (0.0–0.2).
**Cutoff value for trigger PSA was 2.43 ng/mL.
††SD.
‡‡Cutoff value for PSAdt was 7.25 mo.
§§Data are for LR only.
NA = not available; LR = local recurrence; N = lymph node involvement; B = bone metastases; M = distant metastases.

PET/CT performance in patients with PCa recurrence (26). The population was subdivided into 2 groups: group A, including 28 patients with lesion sizes of 5–7.2 mm and a reduction in PSA levels after RT, and group B, including 56 patients with lesion sizes of 7.6–19.4 mm. In group A, the sensitivity, specificity, PPV, and accuracy of PET/CT in identifying local recurrence were 62%, 50%, 88%, and 60%, respectively (26). The diagnostic performance of MRI was better, given that the sensitivity, specificity, PPV, and accuracy were 92%, 75%, 96%, and 89%, respectively (26). Also, in group B, the performance of PET/CT was poorer than that of MRI, given that the sensitivity, specificity, PPV, and accuracy of PET/CT were 92%, 33%, 98%, and 91%, respectively, whereas those of MRI were 94%, 100%, 100%, and 94%, respectively (26).

Lymph Node Recurrence

Few of the studies currently available have assessed the role of 18F-choline PET/CT in detecting recurrence in the lymph nodes. Husarik et al. studied 111 patients who had PCa and underwent 18F-choline PET/CT; 68 of these patients underwent this scan for the purpose of restaging (27). Local recurrence was correctly identified in 36 of 68 patients (27). Twenty-three patients had 18F-choline lymph node uptake, and in 20 of these 23 patients, lymph nodes were surgically removed (27). Histopathology confirmed metastases in all lymph nodes.
nodes but also revealed 2 additional metastases that were not detected by 18F-choline PET/CT. \(T\) i l k i e et al. used 18F-choline PET/CT to study 56 PCa patients who had BR after RP and who subsequently underwent bilateral pelvic or retroperitoneal lymphadenectomy on the basis of positive 18F-choline PET/CT findings. Of 1,149 lymph nodes that were removed and histologically evaluated, 282 (24.5%) harbored metastases. A lesion-based analysis yielded 18F-choline PET/CT sensitivity, specificity, PPV, and NPV of 39.7%, 95.8%, 75.7%, and 83.0%, respectively.

### Bone Metastases

Regarding the diagnostic performance of 18F-choline PET/CT in detecting bone metastases, Beheshti et al. compared the uptake of 18F-fluorocholine in bone metastases in 70 patients before and after treatment for PCa with morphologic changes identified on CT. Overall sensitivity, specificity, and accuracy were 79%, 97%, and 84%, respectively, with lytic lesions showing higher metabolism than sclerotic lesions. The same group compared the potential value of 18F-choline with that of 18F-fluoride in detecting bone metastases in a cohort of 38 patients that included 21 patients with BR and suspected bone metastases. They reported sensitivity, specificity, and accuracy of 74%, 99%, and 85%, respectively, for 18F-choline and 81%, 93%, and 86%, respectively, for 18F-fluoride. Langsteger et al. compared the diagnostic performance of 18F-choline with that of 18F-fluoride (sodium fluoride) and found a significantly higher specificity for 18F-choline than for

### Table 2

**Summary of Studies with 18F-Choline**

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>No. of patients</th>
<th>Type of data collection</th>
<th>PSA (ng/mL)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Assessed parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Median</td>
<td>Range</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cimitan et al. (33)</td>
<td>2006</td>
<td>100</td>
<td>Prospective</td>
<td>1.98*†</td>
<td>0.12–14.3</td>
<td>NA</td>
<td>LR, N, B</td>
</tr>
<tr>
<td>Vees et al. (25)</td>
<td>2007</td>
<td>11</td>
<td>Retrospective</td>
<td>0.35</td>
<td>0.11–0.73</td>
<td>45 (PSA &lt; 1)</td>
<td>LR, N, B</td>
</tr>
<tr>
<td>Pelosi et al. (34)</td>
<td>2008</td>
<td>56</td>
<td>Prospective</td>
<td>4.59*</td>
<td>0.1–39</td>
<td>43</td>
<td>NA</td>
</tr>
<tr>
<td>Beheshti et al. (30)</td>
<td>2008</td>
<td>38</td>
<td>Prospective</td>
<td>56*</td>
<td>74</td>
<td>99</td>
<td>B</td>
</tr>
<tr>
<td>Husarik et al. (27)</td>
<td>2008</td>
<td>111</td>
<td>Prospective</td>
<td>10.81*</td>
<td>86</td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Beheshti et al. (29)</td>
<td>2010</td>
<td>70</td>
<td>Prospective</td>
<td>39.65*</td>
<td>0.1–239</td>
<td>79</td>
<td>97</td>
</tr>
<tr>
<td>Langsteger et al. (31)</td>
<td>2011</td>
<td>42</td>
<td>Prospective</td>
<td>NA</td>
<td>89</td>
<td>96</td>
<td>B</td>
</tr>
<tr>
<td>McCarthy et al. (32)</td>
<td>2011</td>
<td>26</td>
<td>Prospective</td>
<td>10.5</td>
<td>1.6–250</td>
<td>96</td>
<td>96</td>
</tr>
<tr>
<td>Henninger et al. (37)</td>
<td>2012</td>
<td>35</td>
<td>Retrospective</td>
<td>1.33*</td>
<td>0.11–3.06</td>
<td>80*</td>
<td>NA</td>
</tr>
<tr>
<td>Panebianco et al. (26)</td>
<td>2012</td>
<td>84</td>
<td>Prospective</td>
<td>1.17*</td>
<td>0.13–2.94</td>
<td>50</td>
<td>LR</td>
</tr>
<tr>
<td>Schillaci et al. (39)</td>
<td>2012</td>
<td>49</td>
<td>Prospective</td>
<td>4.13*</td>
<td>0.09–15.5</td>
<td>67</td>
<td>NA</td>
</tr>
<tr>
<td>Graute et al. (38)</td>
<td>2012</td>
<td>82</td>
<td>Prospective</td>
<td>2.4</td>
<td>0.03–36</td>
<td>82**</td>
<td>74**</td>
</tr>
<tr>
<td>Chondrogiannis et al. (35)</td>
<td>2013</td>
<td>46</td>
<td>Retrospective</td>
<td>6.5*</td>
<td>1.1–49.4</td>
<td>80††</td>
<td>LR, N, B</td>
</tr>
<tr>
<td>Marzola et al. (40)</td>
<td>2013</td>
<td>233</td>
<td>Retrospective</td>
<td>1.9*††</td>
<td>0.01–20.8</td>
<td>54††</td>
<td>NA</td>
</tr>
<tr>
<td>Beheshti et al. (36)</td>
<td>2013</td>
<td>250</td>
<td>Prospective</td>
<td>46.9*</td>
<td>314.7††</td>
<td>78/81/85/93§§</td>
<td>NA</td>
</tr>
<tr>
<td>Detti et al. (41)</td>
<td>2013</td>
<td>170</td>
<td>Retrospective</td>
<td>16.31</td>
<td>0.5–66</td>
<td>100</td>
<td>57</td>
</tr>
<tr>
<td>Chiaravalloti et al. (42)</td>
<td>2016</td>
<td>79</td>
<td>Retrospective</td>
<td>1.37*</td>
<td>0.21–2</td>
<td>64</td>
<td></td>
</tr>
</tbody>
</table>

*Mean.
†Negative scan results.
‡Positive scan results.
§Patients receiving ADT.
¶Lesion size of 5–7.2 mm.
**Lesion size of 7.6–19.4 mm.
***PSA threshold was 1.74 ng/mL.
††Expressed as rate of detection.
‡‡SD.
§§The different sensitivity values are for different PSA levels: 78 for PSA more than 0.5, 81 for PSA more than 1, 85 for PSA more than 2, and 93 for PSA more than 4.
||PSAdt cutoff value was 6 mo.
NA = not available; LR = local recurrence; N = lymph node involvement; B = bone metastases; M = distant metastases.
INFLUENCE OF PSA ON RATE OF DETECTION BY 18F-CHOLINE PET/CT

As for 11C-choline, the role of 18F-choline has been largely investigated in the setting of BR of PCa, and it appears that the sensitivity of this imaging modality is influenced by PSA levels and PSA kinetics. Cimitan et al. included 100 patients with BR after primary treatment for PCa in a study assessing the role of this imaging modality in detecting recurrent PCa (33). Interestingly, 89% of negative PET/CT scans were obtained in patients with serum PSA levels of less than 4 ng/mL and 87% of such scans were obtained in patients with a Gleason score of less than 8 (33). Pelosi et al. reported a sensitivity of 42.9% in detecting PCa lesions in 56 patients with BR after RP; detection rates increased with increasing PSA levels (20% at PSA levels of <1 ng/mL, 44% at PSA levels of 1–5 ng/mL, and 82% at PSA levels of >5 ng/mL) (34).

More recent studies reported a better rate of detection by 18F-choline PET/CT in patients with BR after RP. Graute et al. reported a positive detection rate of 80.4% in 46 patients with a suspected relapse after RT (35). Similarly to Pelosi et al. (34), this group also found increasing detection rates with increasing trigger PSA levels and reported that the detection rate was not influenced by ADT (35). Similar results were reported by Beheshi et al. in a population of 250 patients with BR; 18F-choline PET/CT detected malignant lesions in 185 of the 250 patients (74%) (36). The sensitivities of 18F-choline PET/CT increased with increasing trigger PSA levels (77.5%, 80.7%, 85.2%, and 92.8% at trigger PSA levels of >0.5, 1.0, 2.0, and 4.0 ng/mL, respectively) and were higher in patients who were receiving ongoing ADT (85%) than in patients who were not (59.5%) (P = 0.001) (36). Other investigators have suggested that ADT may be withheld before examination to reduce the risk of false-negative scans and thereby to increase the rate of detection by 18F-choline PET/CT (5,10,27,37).

Using a cohort of 82 patients with BR after RP, Graute et al. reported a detection rate of 62% and observed that the median PSA level was significantly higher in patients with PET-positive results than in those with PET-negative results (4.3 vs. 1.0 ng/mL; P < 0.01) (38). An optimal PSA threshold of 1.74 ng/mL for detecting recurrent disease was demonstrated by receiver operating characteristic curve analysis (area under the curve, 0.818; 82% sensitivity; 74% specificity) (38). Moreover, significant differences between patients with PET-positive results and those with PET-negative results were found for median PSA levels (6.4 vs. 1.1 ng/mL; P < 0.01) and PSA progression (5.0 vs. 0.3 ng/mL; P < 0.01), with corresponding optimal thresholds of 1.27 and 1.28 ng/mL, respectively (38).

Similar results were reported by Schillaci et al., who found that the rate of detection by 18F-choline imaging was closely related to PSA levels and PSA kinetics (39). In this study, a detection rate of 99% was reported in patients with PSA levels greater than 2 ng/mL, PSAAdt of less than or equal to 6 mo, and PSAvel of less than 2 ng/mL (39). Marzola et al. investigated 233 patients with BR after RP and a high risk for relapse and reported an overall rate of detection by 18F-choline PET/CT of 54%; this rate increased significantly with increasing PSA levels (P < 0.001) (40). Interestingly, patients with positive PET/CT scan results had faster PSA kinetics (mean PSAAdt, 6 mo; mean PSAvel, 9.3 ng/mL/y) than patients with negative PET scan results (mean PSAAdt, 15.4 mo; mean PSAvel, 0.9 ng/mL/y) (40).

Detti et al. evaluated the potential of 18F-choline in 129 patients who underwent PET/CT for the purpose of restaging (41). They observed sensitivity and specificity of 100% and 56.9%, respectively, and found that PSA levels of greater than or equal to 1 ng/mL at the time of restaging were statistically significant predictive factors for PET-positive results, through either univariate analysis (P < 0.0001) or multivariate analysis (P < 0.0001) (41).

Recently, Chiavarotti et al. investigated the performance of 18F-choline in detecting recurrent PCa and its relationship with PSAAdt and PSAvel in 79 patients who were treated with RP and had low PSA levels (<2 ng/mL) (42). They found significant differences in PSAAdt and PSAvel between patients with positive 18F-PET/CT scan results and those with negative 18F-PET/CT scan results (42). Using thresholds of 6 mo for PSAAdt and 1 ng/mL/y for PSAvel, they found detection rates of 65% for PSAAdt of less than or equal to 6 mo and 67% for PSAvel of greater than 1 ng/mL/y (42). These results suggested that 18F-choline PET/CT could be considered for the evaluation of patients with BR of PCa and with low PSA levels and that fast PSA kinetics could be useful in the selection of patients (42).

CONCLUSION

In patients with BR of PCa, either 11C-choline PET/CT or 18F-choline PET/CT has good accuracy in detecting lymph node and distant metastases, with the main advantage of being a single whole-body examination. However, limited accuracy regarding its role in detecting local recurrence is still being reported. The influence of PSA levels and PSA kinetics on the rate of detection by choline PET/CT should always be considered when this examination is performed in order to obtain a better patient selection.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

REFERENCES


25. Vees H, Buchegger F, Albrecht S, et al. [18F]-choline and [11C]-acetate positron emission tomography: detection of residual or progressive subclinical disease at very low prostate-specific antigen values (<1 ng/mL) after radical prostatectomy. BJU Int. 2007;99:1415–1420.


11C- or 18F-Choline PET/CT for Imaging Evaluation of Biochemical Recurrence of Prostate Cancer

Paola Mapelli, Elena Incerti, Francesco Ceci, Paolo Castellucci, Stefano Fanti and Maria Picchio

Doi: 10.2967/jnumed.115.169755

This article and updated information are available at:
http://jnm.snmjournals.org/content/57/Supplement_3/43S

Information about reproducing figures, tables, or other portions of this article can be found online at:
http://jnm.snmjournals.org/site/misc/permission.xhtml

Information about subscriptions to JNM can be found at:
http://jnm.snmjournals.org/site/subscriptions/online.xhtml